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STUDIES OF HYPOVITAMINOSIS A

III. CLINICAL EXPERIMENTS IN THE VITAMIN A BALANCE IN CHILDREN AFTER VARIOUS DIETS

C. FRIDERICHSEN, M.D.
AND
C. EDMUND, M.D.
COPENHAGEN, DENMARK

In the preceding studies of hypovitaminosis A in children we [1] indicated a clinical method of measuring the reflex irritability of the eye to light when both the child and the experimenter are perfectly adapted to darkness. We called this measurable magnitude the minimum reflexible.

Just as it is possible by measuring the degree of hemeralopia in the older child and the adult to demonstrate latent hypovitaminosis A, it is possible by measuring the minimum reflexible of the young child to obtain a quantitative expression for the vitamin A deposited in the organism.

Since we were able to detect a distinctly measurable reduction of the minimum reflexible in a series of children under 1 year of age who had for some time received a diet poor in vitamin A, and since that reduction lessened immediately after a single therapeutic dose of a vitamin A preparation, we think it justifiable to use this method when we wish to decide whether a child has an adequate vitamin A content.

As we had, moreover, detected a reduction of the minimum reflexible in certain diseases, such as celiac disease and some forms of dystonia, we thought that the reduction must be due to inefficiency in the resorption of vitamin A in the form in which it is administered. At the present stage of our investigations, therefore, we may presume that a reduction of the minimum reflexible in a child under 1 year old

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From the pediatrics department of the Sundby Hospital, C. Friderichsen, senior physician.

1. Friderichsen, C.: Studies of Hypovitaminosis A: I. Quantitative Investigations of the Resorption of A Vitamin in a Case of Celiac Disease, Acta pædiat. **18**:377, 1936. Friderichsen, C., and Edmund, C.: II. A New Method for Testing the Resorption of Vitamin A from Medicaments, Am. J. Dis. Child. **53**:89 (Jan.) 1937.

suggests a slight deficiency of vitamin A, i. e., hypovitaminosis A, and that we can determine its degree by measuring the minimum reflexible. In the following paragraphs we shall endeavor to show the effect of different forms of diet on the vitamin A content of infants.

CLINICAL EXPERIMENTS WITH DIFFERENT FORMS OF DIET

In our experiments we employed several of the diets which are administered to young infants: a water diet (inanition diet), a buttermilk diet, a protein milk diet, a diet consisting of Nestlé's children's food, a diet minus animal fat and an ordinary mixed diet. In addition we examined the value of carrots administered either as carrot juice or as mashed carrots. In order that we might profit as much as possible by the experiments, we frequently combined a special diet with medication. Each chart contains curves showing the results of one type of experiment.

EXPERIMENTS WITH WATER DIET

After a series of experiments with a water diet we reached the following preliminary conclusion: A water diet of twenty-four, thirty-six or forty-eight hours' duration, such as is generally employed in this type of therapy, causes a gradual reduction of the vitamin A content of the organism. The younger the child the more distinctly and the more rapidly does the reflex irritability to light decrease during inanition. In healthy children of from 2 to 6 months a reduction of the minimum reflexible from 6.00 to 5.50 or 5.25 is the usual result of a water diet of forty-eight hours' duration.

In older, stronger children, who have received a mixed diet containing many vegetables, the content is relatively fixed, and the detected reduction, therefore, may be slight. In small, atrophic children the vitamin A content is low, and a water diet has so strong an effect that hypovitaminosis A ensues almost immediately. In children already suffering from hypovitaminosis A, whose minimum reflexible is reduced, this condition is greatly exacerbated by a water diet of twenty-four or forty-eight hours' duration.

Thus, we employed the water diet as a kind of functional test which enabled us to ascertain the magnitude of the reserve content of vitamin A in the organism. Just as we could rapidly increase the content by the administration of vitamin A preparations, we could bring about a diminution in the vitamin A required by the organism for its adequate function. The younger the child the less it is able to store up vitamin A. A protracted water diet, therefore, implies a risk, notably with children who have previously been treated with a diet deficient in protein and whose vitamin A content is consequently diminished. This is a factor of which previous experimenters have not been aware.

A few of our results agree, however, with those which Debré and Busson [2] derived from examinations of the organs of dead children.

EXPERIMENTS WITH BUTTERMILK AND PROTEIN MILK

To the buttermilk were added 1 or 2 per cent of flour and 3 or 4 per cent of sugar, and the fat content of all the milk mixtures was controlled twice a week. The fat content of the buttermilk varied between 0.1 and 0.4 per cent and that of the protein milk between 2.3 and 2.5 per cent; that of the children's milk amounted to 3.8 per cent.

CASE 1.—*Water diet and buttermilk diet.*

A boy aged 4 months was admitted to the hospital on Aug. 1, 1934, and was dismissed on Nov. 3, 1934. The diagnosis was exudative lymphatic diathesis, bronchitis and dystrophia.

In connection with subfebrile bronchitis in the overfat child, who was suffering from eczema, diarrhea and dystrophia developed. At home he had been fed a milk mixture and a vitamin D preparation; in the hospital he received barley water for twenty-four hours and, subsequently, increasing amounts of the buttermilk mixture. The test performed on August 15 revealed severe hypovitaminosis A; the minimum reflexible, only a fortnight after the institution of treatment showed the low value of 4.75. As the stools during this treatment had become normal, the buttermilk diet was continued in order that we might see whether it aggravated the hypovitaminosis. However, since the dyspepsia was cured, the patient was able not only to resorb the slight amount of vitamin A contained in the buttermilk but even to increase his vitamin content. During the next fortnight the minimum reflexible rose from 4.75 to 5.25 without the administration of any vitamin A supplement. As diarrhea again developed, the boy was treated by inanition for twenty-four hours. The water diet immediately reduced the vitamin A content, for the minimum reflexible was reduced to 5.00. Subsequently, the boy received 250 Gm. of sweet milk (3.8 per cent fat) besides the buttermilk, and since this agreed with him, the buttermilk diet was abandoned. In its place he received an ordinary mixed diet containing 500 Gm. of sweet milk a day. The hypovitaminosis immediately disappeared, without the patient's receiving any supplement of vitamin A. However, on account of dyspepsia the buttermilk mixture plus 250 Gm. of sweet milk had to be reverted to. This time no reduction in the light reflex was witnessed. The vitamin A content was normal.

Results.—A water diet of twenty-four hours' duration and the subsequent administration of a buttermilk mixture in increasing amounts caused severe hypovitaminosis A in a child with fever and diarrhea. When the diarrhea was cured, the organism was able to retain the minimal quantity of fat contained in the buttermilk. The hypovitaminosis was aggravated by a water diet of twenty-four hours' duration, but immediately yielded to an ordinary mixed children's diet, which was instituted in place of the buttermilk diet.

2. Debré, R., and Busson, A.: Rev. franç. de pédiat. **10**:413, 1934.

CASE 2.—*Experiment with a twin; buttermilk and protein milk diet.*

A boy aged 3 months was admitted to the hospital on Oct. 3, 1934, and was dismissed on Jan. 12, 1935. The diagnosis was atrophy due to inanition and eczema capitis.

The patient was a twin weighing 2,000 Gm. below normal. He had been receiving a little mother's milk and a milk mixture, but had not thrived. Since he had had fatty stools and diarrhea while he was on the milk diet, as well as eczema of the scalp, he was given a buttermilk diet. A test of the eyes revealed a slight reduction in the minimum reflexible, which increased after three weeks of treatment with buttermilk. After ten days of a diet of protein milk, which contains somewhat more fat, but without any supplementary fat, the slight hypovitaminosis disappeared.

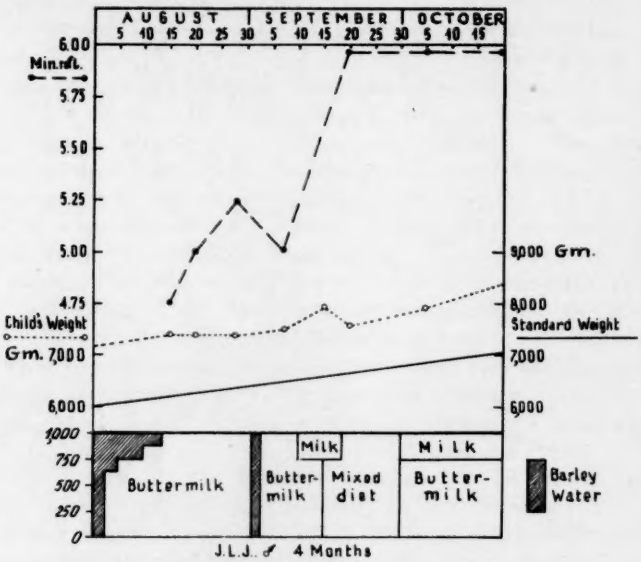

Chart 1.—Data in case 1.

Result.—Hypovitaminosis A was observed in an atrophic twin who had been treated with buttermilk because of a tendency to dyspeptic stools. The condition yielded to treatment with protein milk, and the stools became normal.

CASE 3.—*Experiment with a twin; buttermilk and protein milk diet.*

The patient was a boy aged 3 months. The diagnosis was atrophy due to inanition and eczema capitis.

The history was similar to that in case 2, but the child was much sicker than his brother. A test of the eyes revealed a slightly reduced minimum reflexible, which was exacerbated after three weeks of a buttermilk diet. Since the dyspepsia persisted, the child was given protein milk, after which treatment the hypovitaminosis improved somewhat. However, since the minimum reflexible, in contradistinction to that of his brother, continued to be lower than normal after three weeks, he was given 10 drops of a preparation of halibut liver oil

(2,850 international, or U. S. P., units of vitamin A) two times, after which the minimum reflexible immediately became normal. He was cured only when he received mother's milk.

Result.—In an atrophic twin with chronic diarrhea (decomposition) the hypovitaminosis was exacerbated by a buttermilk diet. The dyspepsia and hypovitaminosis were somewhat improved by the administration of protein milk, but only when the child received a supplementary dose of vitamin A factor did the hypovitaminosis disappear.

CASE 4.—*Buttermilk diet, with mashed carrots.*

A boy aged 4 months was admitted to the hospital on Sept. 17, 1934, and was dismissed on Oct. 31, 1934. The diagnosis was acute dyspepsia with dystrophia.

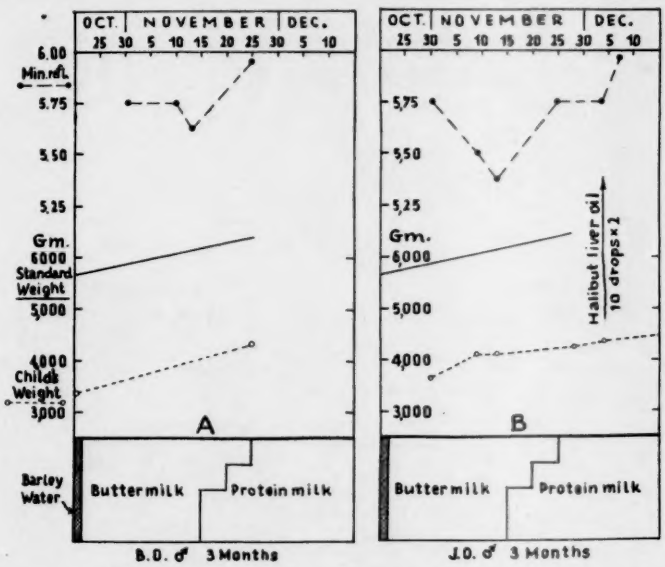

Chart 2.—*A*, data in case 2; *B*, data in case 3.

At home diarrhea had always developed in the patient after he received a milk mixture. He was therefore given buttermilk for three weeks. Consequently, his minimum reflexible was reduced to 5.50. Since the diarrhea ceased, the buttermilk diet was continued, and the minimum reflexible improved. Thus the child was able to increase his vitamin A content by means of buttermilk alone, although it is poor in fat. However, since the content did not become entirely normal, a fact which was detected by means of subsequent tests of the eyes, the boy was given 90 Gm. of mashed carrots (about 1,800 international, or U. S. P., units of vitamin A) (30 Gm. three times), which restored his minimum reflexible to normal.

Result.—A buttermilk diet cured dyspepsia, and the hypovitaminosis A improved, but mashed carrots caused it to disappear entirely.

This is an instance of the typical effect of the ingestion of carrots. We shall record several cases in which carrots did not affect the vitamin A content and consequently the minimum reflexible of the eye.

CASE 5.—*Water diet, buttermilk and protein milk diet.*

The patient, a girl, aged 3 months, was admitted to the hospital on Aug. 8, 1934, and was dismissed on Oct. 1, 1934. The diagnosis was acute dyspepsia with dystrophia.

The patient was treated first with a buttermilk diet, which did not, however, alleviate the diarrhea. A reduction of the minimum reflexible, to 5.75, had already been detected. The diet was therefore changed, and gradually increasing amounts of protein milk were given. The minimum reflexible underwent a further decrease, going down to 5.25, and this value persisted for ten days. The administra-

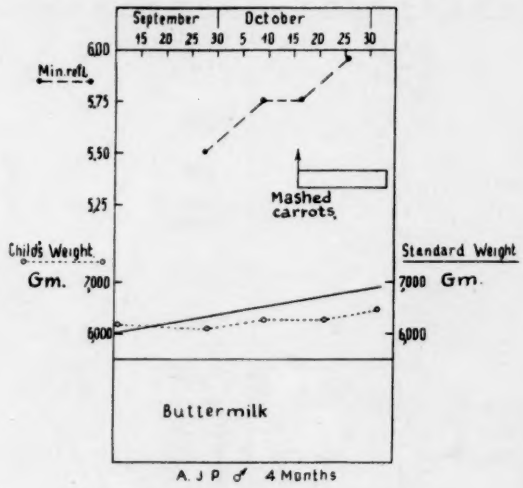

Chart 3.—Data in case 4.

tion of 250 Gm. of cow's milk resulted in a new period of diarrhea. This diet was therefore discontinued, and the child was given barley water for twenty-four hours, after which the protein milk diet was reinstituted. The weight of the patient did not vary. Owing to the repeated periods of inanition, the vitamin A content of the patient was so severely decreased that the minimum reflexible was reduced to 4.75. Since the stools had become normal, she was given an ordinary mixed children's diet plus 20 drops of a preparation of halibut liver oil a day (5,700 international, or U. S. P., units of vitamin A). This treatment gave rise to an increase in weight and an improvement in the minimum reflexible, which rose from 4.75 to 5.50, but despite the diet rich in vitamin A and the preparation of halibut oil, the minimum reflexible did not attain its normal value in the course of a fortnight. Thus, the vitamin A administered either was not sufficient to saturate the content in the course of a fortnight or was not entirely resorbed. Unfortunately, the experiment was interrupted because the child was taken out of the hospital.

Result.—If dyspepsia persists and is accompanied by loss of weight during a buttermilk or protein milk cure, the hypovitaminosis is exacerbated. By a water diet of twenty-four hours' duration, the vitamin A content of the organism is decreased still further. After protracted and severe dyspepsia more than a fortnight is required before the content is replenished by means of mixed diet plus 5,700 international (U. S. P.) units of vitamin A in the form of a preparation of halibut liver oil.

CASE 6.—*Protein milk diet with carrot juice.*

B. J., aged 4 months, was admitted to the hospital on July 14, 1934, and dismissed on Oct. 11, 1934. The diagnosis was universal eczema and dystrophia.

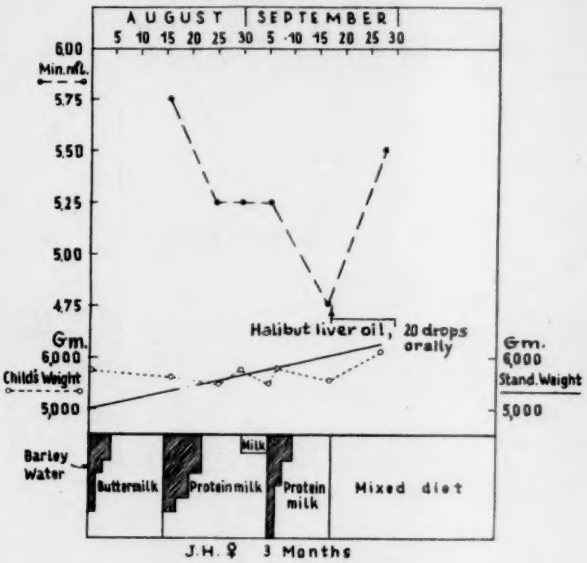

Chart 4.—Data in case 5.

For a fortnight prior to admission the patient had continual diarrhea. The body weight was 1,500 Gm. below normal. The patient had extensive weeping eczema, which improved after treatment with buttermilk. However, since the stools continued to be liquid and the weight did not increase, a protein milk diet was instituted. This brought about an improvement in the stools. After about sixteen weeks of this diet, which was comparatively poor in fat, the dark room test revealed a reduction in the minimum reflexible, the severity of which increased despite the daily administration of 45 Gm. of carrot juice (about 900 international, or U. S. P., units of vitamin A) for about a fortnight. After another fortnight, during which the child received a mixed children's diet, with about 650 Gm. of milk a day, the minimum reflexible was restored to its normal value. The weight, which had been stationary during the period in which whole protein milk was given, began to increase with the administration of carrot juice. The sensitivity to light, however, was not influenced.

Result.—A diet initially consisting of buttermilk and subsequently supplemented with protein milk, administered for about six weeks, provoked hypovitaminosis in a child suffering from chronic dyspepsia (dystrophia). Despite the daily administration of 45 Gm. of carrot juice (about 900 international, or U. S. P., units of vitamin A), the hypovitaminosis was exacerbated, and it had not disappeared after a fortnight during which the child received the ordinary mixed children's diet.

EXPERIMENT WITH CHILDREN'S FOOD

CASE 7.—A girl aged 2 months was admitted to the hospital on Sept. 3, 1934, and dismissed on Nov. 6, 1934. The diagnosis was acute dyspepsia and dystrophia.

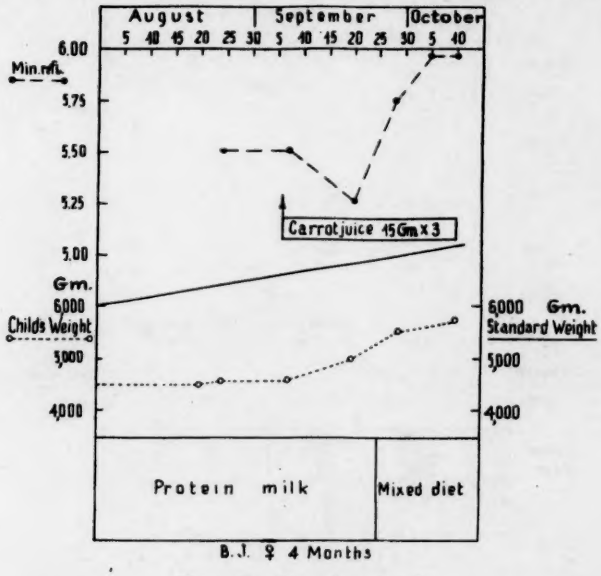

Chart 5.—Data in case 6.

The patient was at once given a buttermilk diet, but it did not agree with her, and the diarrhea recurred. Weak milk mixtures were then tried, but they did not agree with her either. After a barley water diet of twenty-four hours' duration, Nestlé's children's food was resorted to; during this treatment the diarrhea stopped, but the child's weight remained stationary. Unfortunately, examination of the eyes had to be postponed because of infection in the sick-room. The patient was then given a milk mixture, which was gradually made more concentrated. After ten days' treatment, examination of the eyes revealed a reduction of the minimum reflexible, despite the administration of 500 Gm. of milk a day. Thus, in a dystrophic child a diet of children's food provoked hypovitaminosis, which, during the subsequent days, yielded to the administration of a milk mixture without any supplement of vitamin A. At the same time, the child's weight increased.

Result.—A dystrophic child receiving a diet of Nestlé's children's food contracted hypovitaminosis A, which disappeared after the administration of 500 Gm. of milk daily for about twenty days.

EXPERIMENTS WITH A DIET MINUS ANIMAL FAT

A diet minus animal fat, which was indicated by Monrad [3] for the treatment of exudative lymphatic diathesis, is in many instances the only diet to which this symptom complex will yield. It must be mentioned, however, that the diet which we employed did not correspond to that indicated by Monrad, since in some experiments we deliberately excluded carrots, spinach and tomatoes and the mashed potatoes were

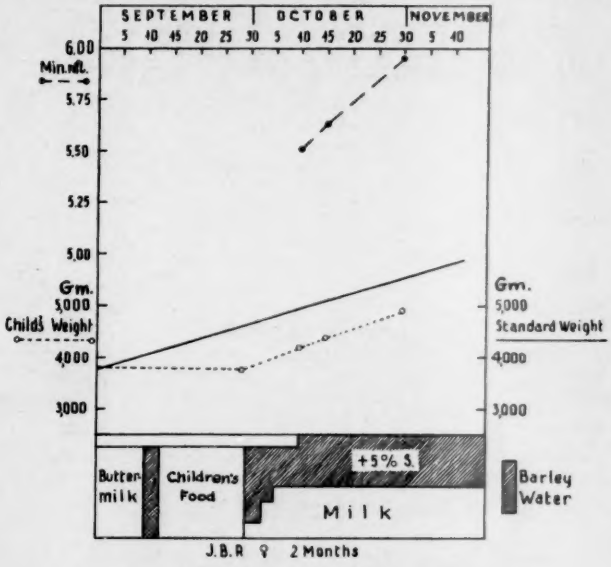

Chart 6.—Data in case 7. "S." indicates sugar.

not stirred up with milk. This was done because we wanted to find out whether an extra supply of carrot juice or of mashed carrots could furnish the vitamin A requirements.

CASE 8.—*Diet minus animal fat, without carrots and spinach.*

A boy aged 7 months was admitted to the hospital on June 3, 1934, and dismissed on Sept. 22, 1934. The diagnosis was eczema of the face, exudative lymphatic diathesis and anemia.

As the eczema was exacerbated after two weeks' treatment with an ordinary mixed diet (including 500 Gm. of milk) and the child's weight exceeded the normal by about 1,500 Gm., the diet was changed to the diet minus animal fat (without carrots or spinach). The weight continued to increase gradually, and the minimum reflexible after one month showed a normal value. This value decreased, however, after about six weeks of the diet. The weight continued

3. Monrad, S. V.: Acta pædiat. **1**:271, 1921.

to increase, but the eczema yielded to treatment. After the patient had received an ordinary mixed diet without a supplement of vitamin A, for a fortnight, the examination revealed a normal light sense; the eczema, however, had recurred because of the diet rich in milk.

Result.—After six weeks' treatment with a diet minus animal fat and without carrots and spinach, the patient incurred hypovitaminosis A, which yielded to treatment with an ordinary mixed diet.

CASE 9.—*Diet minus animal fat, combined with carrots.*

A girl aged 11 months was admitted to the hospital on Nov. 27, 1934, and dismissed on Feb. 6, 1935. The diagnosis was exudative lymphatic diathesis.

The child, whose weight exceeded the normal by about 1,700 Gm., was treated with a diet minus animal fat. After about three weeks' examination of the eyes

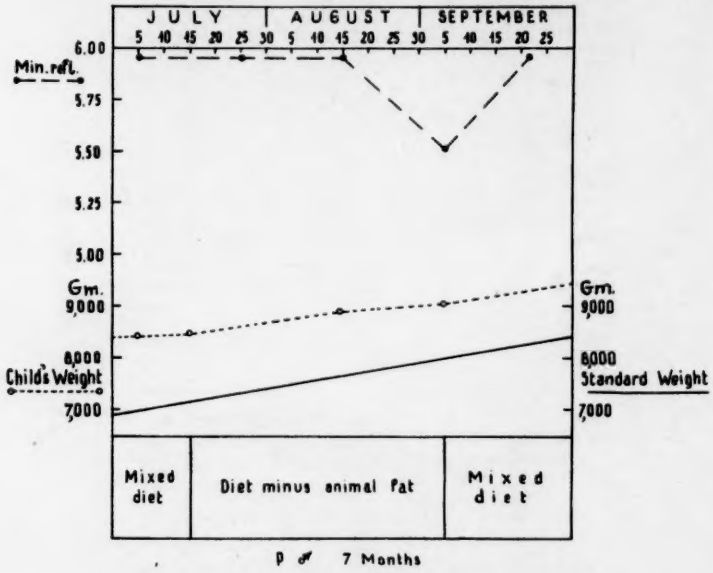

Chart 7.—Data in case 8.

she revealed a reduction in the minimum reflexible, which persisted during the following twenty-five days despite the administration of 75 Gm. of carrot juice a day during the last fortnight. Thus, the patient was unable to resorb the vitamin A from the carotene of the carrots. She presented no dyspeptic symptoms to explain the faulty resorption. In order to ascertain the lability of the vitamin A content of the patient, we gave her a water diet for twenty-four hours. This promptly reduced the minimum reflexible to 4.50. During the following two days the child received a diet minus animal fat, which, despite its scanty vitamin A content, brought about a slight improvement in the minimum reflexible. It did not however, restore the vitamin A content to its previous condition. The patient was therefore given an isolated dose of 20 drops of the preparation of halibut liver oil by mouth (5,700 international, or U. S. P., units of vitamin A). Twenty-five minutes later the minimum reflexible was normal. This normal value persisted for three days, after which the vitamin A content decreased

again. After eight days the child had hypovitaminosis, although she had received 75 Gm. of carrot juice every day. She was therefore given 3 Gm. of a preparation of dried spinach (300 international, or U. S. P., units of vitamin A), which is so rich in carotene and the effect of which is as speedy as that of the preparation of halibut liver oil, though it is perhaps somewhat less intense. At any rate, after thirty-five minutes the content was restored almost to normal, where it remained somewhat longer than it had after the administration of the preparation of halibut liver oil, i. e., for ten days.

Results.—Three weeks' treatment with a diet minus animal fat gave rise to hypovitaminosis A; 1,500 international (U. S. P.) units

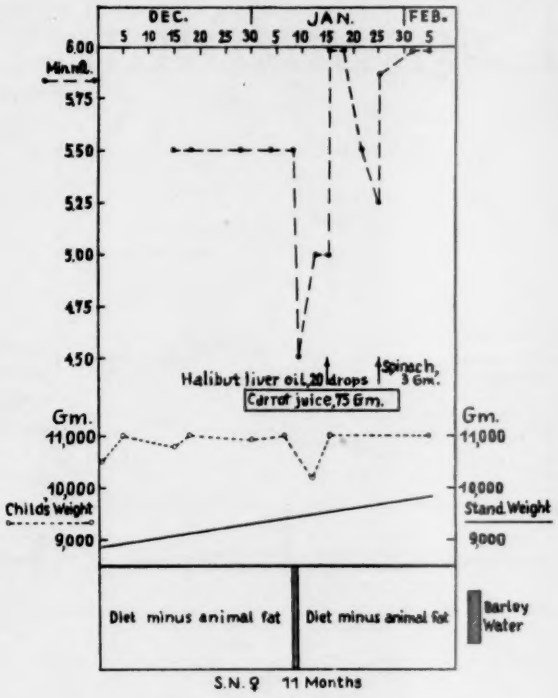

Chart 8.—Data in case 9.

of vitamin A administered daily in the form of carrot juice was not resorbed, although the patient never presented any dyspeptic symptoms. The hypovitaminosis yielded immediately both to the preparation of halibut liver oil (5,700 international, or U. S. P., units of vitamin A) and to the preparation of spinach (300 international, or U. S. P., units of vitamin A). The effect of the spinach preparation was of longer duration than that of the halibut liver oil preparation. Hence, there is a difference in the action exerted by the carotene contained in carrots and that exerted by the carotene contained in spinach.

CASE 10.—*Diet minus animal fat, combined with carrots.*

A boy aged 9 months was admitted to the hospital on June 26, 1934, and dismissed on Oct. 3, 1934. The diagnosis was exudative lymphatic diathesis, eczema and chronic catarrh.

During a preliminary experimental period of twenty days the patient received an ordinary mixed diet plus two doses of 8 drops of the preparation of halibut liver oil (2,280 international, or U. S. P., units of vitamin A). Since both the eczema and the catarrh were exacerbated and since it had been ascertained that the minimum reflexible was normal, the diet minus animal fat was administered, but without carrots and spinach. After twenty days the child had hypovitaminosis A, which was evidenced by the reduction in the minimum reflexible from 6.00 to 5.25. This condition persisted for five days, after which the child was given

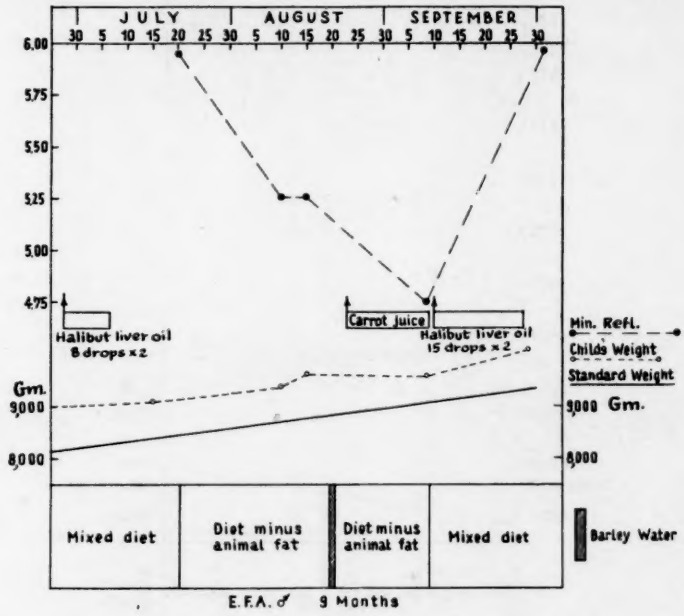

Chart 9.—Data in case 10.

a water diet for twenty-four hours because of diarrhea. Subsequently, he was again given the diet minus animal fat. As it was known from previous experiments that treatment by inanition during a period of hypovitaminosis is likely to increase the hypovitaminosis, the patient was given 150 Gm. of carrot juice a day. However, the carotene contained in the carrot juice evidently was unable to prevent a further depletion of the vitamin A content, for the minimum reflexible, despite a fortnight's treatment with carrot juice, was reduced to 4.75. Since it was not considered expedient to continue the treatment with the diet minus animal fat, and since the eczema had disappeared, the patient was given a mixed diet plus two doses of 15 drops of the preparation of halibut liver oil (4,275 international, or U. S. P., units). After twenty days the minimum reflexible was restored to its normal value but both the eczema and the catarrh had recurred. The experiment had to be interrupted.

Result.—A diet minus animal fat brought about hypovitaminosis in the course of twenty days. The hypovitaminosis was greatly exacerbated by twenty-four hours of a water diet. The daily administration for a fortnight of 3,000 international (U. S. P.) units of vitamin A in the form of carrot juice did not produce any improvement in the hypovitaminosis, but it yielded to an ordinary mixed diet supplemented with a preparation of halibut liver oil.

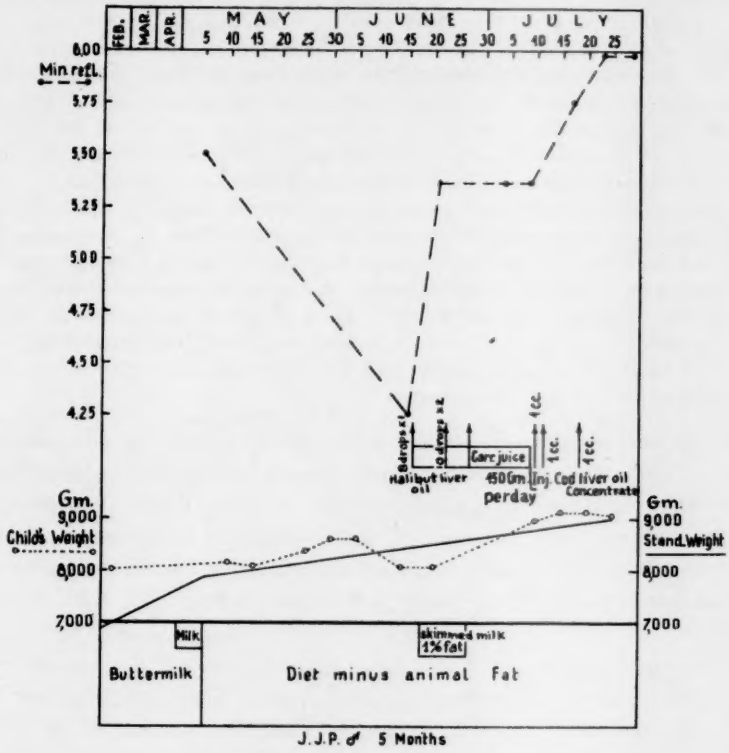

Chart 10.—Data in case 11.

CASE 11.—*Diet minus animal fat, combined with carrots and parenteral injections.*

The patient was a boy aged 5 months.

The diagnosis was exudative lymphatic diathesis and universal eczema.

The child had been nursed till admission. During the previous three months he had had severe eczema, which was aggravated when he received any other food than buttermilk. Moreover, at every change of diet he had incurred diarrhea, and it had therefore been necessary to continue with the buttermilk diet during the months of February, March and April. At the beginning of May we tried giving the patient 100 Gm. of cow's milk, but this immediately exacerbated the eczema and the dyspepsia. After the three months of a buttermilk diet the value of the minimum reflexible was found to be only 5.50, and the boy was therefore given a

diet minus animal fat and without carrots. This diet brought about a gradual increase in weight. Every time the boy received a slight supplement of fat in the form of milk pottage (1 per cent of fat) his eczema recurred or diarrhea developed. The examination of the eyes performed on June 15 revealed a considerable reduction in the minimum reflexible to 4.25, which indicated that the hypovitaminosis had become worse. The patient presented no signs of xerosis and the cornea was normal, but the eyelids and the borders of the eyelids were somewhat red. He presented also some photophobia. There were no Bitot spots, but the urine contained isolated epithelial cells. The patient was given 8 drops of the preparation of halibut liver oil (2,280 international, or U. S. P., units of vitamin A). As the minimum reflexible after eight days was only 5.50, the patient was given two doses of 10 drops of the halibut liver oil preparation (5,700 international, or U. S. P., units of vitamin A) and, at the same time, 300 Gm. of half skimmed milk (1 per cent of fat). This increase in vitamin A was not sufficent to bring about an improvement in the minimum reflexible, and an increase in the amount of the preparation administered provoked diarrhea. This treatment was therefore discontinued and 150 Gm. of mashed carrots (about 3,000 international, or U. S. P., units of vitamin A) daily was given instead, without, however, producing the desired effect. As an increase in the dose of the halibut liver oil preparation and in the administration of cow's milk caused diarrhea, we had to give up supplying the patient with vitamin A in those forms. We therefore endeavored to obtain a better result by parenteral injection of 1 cc. of cod liver oil concentrate (about 1,000 international, or U. S. P., units of vitamin A), which was repeated two days later. The minimum reflexible rose to 5.75, but it was not restored to normal until a third injection had been administered.

Result.—A buttermilk diet and a diet minus animal fat administered for four and one-half months caused severe, latent avitaminosis with prexerotic symptoms. The administration of small doses of a preparation of halibut liver oil and of half skimmed milk only partially corrected the condition, and no effect was obtained by the daily administration for a fortnight of about 3,000 international (U. S. P.) units of vitamin A in the form of carrot juice. Not before several parenteral injections of vitamin A in the form of cod liver oil concentrate had been administered was any effect perceptible. This indicates that the power of resorption had been deficient. Thus, this patient had a mixed form of exogenous and endogenous hypovitaminosis A, for which the diet and the faulty resorption were each partly responsible.

CASE 12.—*Diet minus animal fat, combined with carrots and milk.*

A boy aged 11 months was admitted to the hospital on Nov. 8, 1934, and dismissed on May 5, 1935.

The diagnosis was exudative lymphatic diathesis, acute otitis media and eczema.

The weight of the patient was about 2,000 Gm. above normal. He was treated with a diet minus animal fat because of recurring nasal, aural and bronchial catarrh. After six weeks a reduction in the minimum reflexible (to 5.00) was detected. The patient gained weight during the treatment. He was then given 150 Gm. of mashed carrots a day (about 3,000 international, or U. S. P., units of vitamin A) for about one month, but repeated examinations revealed no improvement in his minimum reflexible. The administration of carrots was therefore

discontinued, and one dose of 2 Gm. of the preparation of dried spinach (about 200 international, or U. S. P., units of vitamin A) was administered. Immediately afterward the lassitude and indolence of the child were relieved. The effect of this isolated dose disappeared after about sixteen days. The minimum reflexible decreased, and after about eight weeks it showed the same low value as it had prior to the administration of the spinach preparation. Renewed administration of 150 Gm. of mashed carrots a day for a month produced no effect, and the child became dull again. However, when he received 100 Gm. of cow's milk a day (about 100 international, or U. S. P., units of vitamin A), his minimum reflexible immediately improved and it was soon restored to normal. When dismissed he was on an ordinary mixed diet.

Result.—A diet minus animal fat administered for six weeks caused hypovitaminosis A. The daily administration of about 3,000 inter-

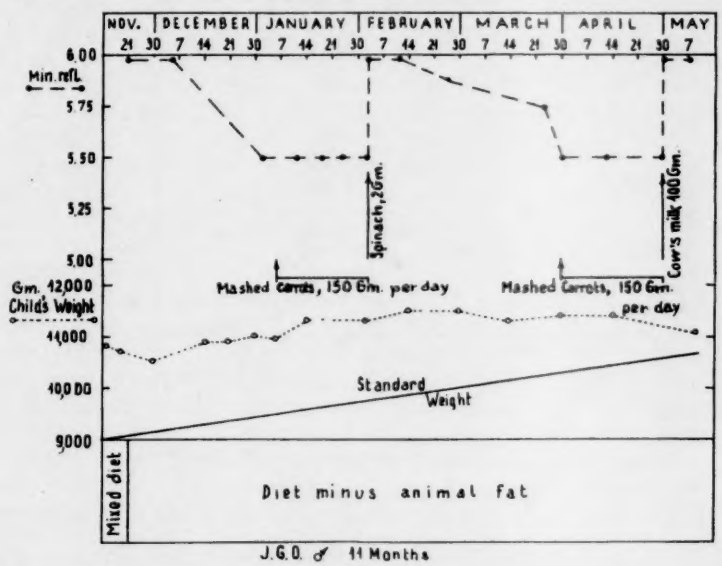

Chart 11.—Data in case 12.

national (U. S. P.) units of vitamin A in the form of mashed carrots was without effect. An isolated dose of 2 Gm. of a preparation of spinach (about 200 international, or U. S. P., units of vitamin A) immediately brought about an improvement. Not for eight weeks was the effect of the single dose of dried spinach exhausted. A supplement of 100 Gm. of milk (about 100 international, or U. S. P., units of vitamin A) caused the hypovitaminosis to disappear. It is evident that the carotene contained in carrots and that contained in spinach have a different effect.

CASE 13.—*Diet minus animal fat, combined with carrots and milk.*

The patient in this case was the same as the patient in case 12. He was readmitted to the hospital at the age of 18 months, on May 15, 1935, and was dismissed on Sept. 16, 1935. The diagnosis was exudative lymphatic diathesis and eczema.

The child was readmitted because of recurring catarrh after he had received an ordinary mixed diet plus 500 Gm. of milk for ten days. He was therefore given the diet minus animal fat again. During the following six weeks his minimum reflexible remained normal. It was evident that the previous hypovitaminosis had disappeared and that the vitamin A content had been saturated by the mixed diet administered for ten days. Two months after the institution of the diet minus animal fat, a reduction in the minimum reflexible was detected. The patient was therefore treated with 150 Gm. of mashed carrots a day (about 3,000 international, or U. S. P., units of vitamin A), though without any effect. On Aug. 30 he received 100 Gm. of cow's milk, which did not suffice, however, to increase the light sense. No improvement was witnessed before the patient was given the ordinary mixed diet.

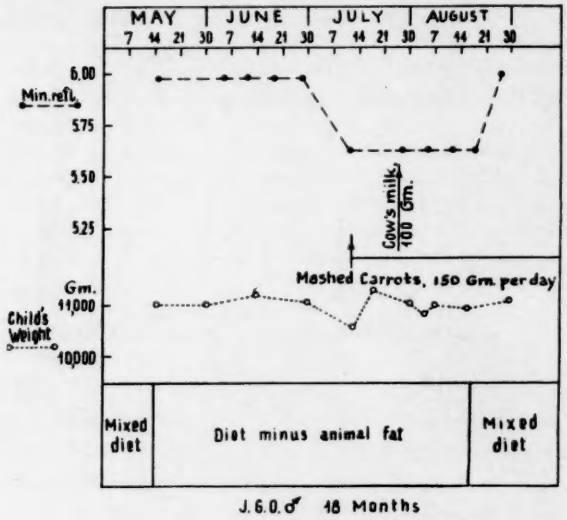

Chart 12.—Data in case 13.

Result.—A diet minus animal fat administered for seven weeks caused hypovitaminosis. The daily administration for one month of about 3,000 international (U. S. P.) units of vitamin A in the form of mashed carrot juice had no effect. Nor did an isolated dose of 100 Gm. of cow's milk produce any effect this time. The hypovitaminosis yielded to the administration of an ordinary mixed children's diet.

CASE 14.—A boy aged 4½ months was admitted to the hospital on Nov. 11, 1934, and dismissed on Feb. 16, 1935. The diagnosis was dystrophia.

The patient had been nursed during the first three months. He was then given a diet consisting of water gruel and a little buttermilk, but only because of abnormal stools. He was fairly strong, though underfed, and had no sign of carbohydate dystrophia. After twenty-four hours on a water gruel diet he received 50 per cent milk and water with 5 per cent sugar. After two days his minimum reflexible was reduced to 5.50, and after another four days it was still lower, despite the daily administration of 500 Gm. of cow's milk and despite the absence of dyspepsia.

He was therefore given 16 drops of the preparation of halibut liver oil (4,560 international, or U. S. P., units of vitamin A) daily. However, since his fecal discharges after three days became frequent, liquid, fatty and saponaceous, the halibut liver oil and the diet were discontinued and he was given barley water for ten hours. Subsequently, examination of the eyes revealed a considerable reduction in the minimum reflexible (to 4.50). At the same time, the conjunctivae became finely wrinkled (prexerotic?).

A reduction in the vitamin A content after a water diet of such a few hours' duration suggested that the patient had not resorbed either the halibut liver oil preparation or the fat contained in the milk. Moreover, since he presented prexerotic symptoms, the oral administration of vitamin A was discontinued and was replaced by an intramuscular injection of cod liver oil concentrate (about 1,000 international, or U. S. P., units of vitamin A). Five minutes after the injection the minimum reflexible showed an improvement, and after fifteen minutes it had attained the value of 5.50. Evidently the dose had not been sufficient to raise the minimum reflexible to normal. However, the conjunctivae had become normal, and the child was much livelier and reacted promptly to the irritant. During the buttermilk diet the stools became normal. The effect of the isolated injection persisted for about eight days, after which it decreased again, for the minimum reflexible was reduced to 5.25, where it persisted for three days.

As the diarrhea recurred, the child was given barley water for twenty-four hours, after which the minimum reflexible was again reduced. However, this time the reduction was not so great as it had been on the previous occasion. This suggests that the intramuscular injection of vitamin A exerts a stronger and more protracted effect than the oral administration.

Light therapy was then resorted to, though without its producing any effect on the minimum reflexible. The patient received three doses of 10 Gm. of carrot juice. As the light sense did not improve, the amount given was increased to three doses of 50 Gm. (3,000 international, or U. S. P., units of vitamin A), which brought about an improvement during the following days. Although the carrot juice was not able to saturate the vitamin A content, the child became surprisingly lively and brisk. Despite the great daily dose, of about 3,000 international (U. S. P.) units of vitamin A, administered for sixteen days at a time when there was no dyspepsia, the minimum reflexible did not attain its normal value. Therefore, the patient was given 0.5 Gm. daily for four days of the preparation of spinach, i. e., about 100 international (U. S. P.) units of vitamin A daily, after which the minimum reflexible became normal. The administration of the spinach preparation was discontinued, but the effect persisted for eight days. Subsequently, the minimum reflexible began to oscillate between 5.75 and 6.00. When the child received 350 Gm. of cow's milk it returned to normal. However, the milk diet did not agree with the child, for after eight days the diarrhea recurred. Barley water was then given for eighteen hours. The vitamin A content was again reduced, and the minimum reflexible could not reach its normal value because we dared not give the boy more than 200 Gm. of cow's milk a day. Since his weight increased, he was dismissed.

Result.—This case represents a mixed form of exogenous and endogenous hypovitaminosis A, which was due partly to the diet and partly to deficient resorption, for despite the administration of cow's milk and a halibut liver oil preparation, prexerotic symptoms appeared and persisted until a cod liver concentrate (about 1,000 international,

or U. S. P., units of vitamin A) was administered parenterally. The vitamin A content due to the isolated injection was exhausted after eight days.

This case is particularly interesting and illustrative, for it shows the astounding accuracy of the method of determining the minimum reflexible of the eye when this is done by an expert.

Of a clinical method of this kind one is bound to be skeptical and critical. That is why Edmund, both in these and in all the other experiments, was kept in ignorance as to what treatment the patient received.

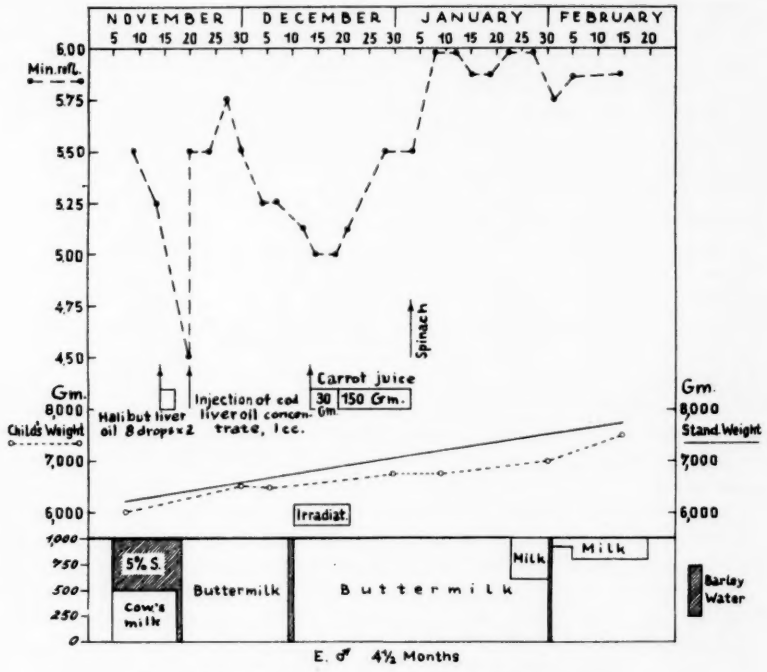

Chart 13.—Data in case 14. "S." indicates sugar.

However, not only can most of the reactions be logically explained by the changes in the diet or by the medication, but the appearance of prexerotic symptoms and the psychic changes observed in the last patients agree with the reactions witnessed during the dark room test and after the medicamental therapy.

Suggestion could hardly have played a part, because at every test there were seven or eight children in the dark room, some of them being control subjects. When we administered the cod liver oil concentrate to the patient in case 14, another child suffering from hypovitaminosis received a simultaneous injection of a medicine containing no vitamin A, but in both cases the reaction of the eyes was unmistakable.

CONCLUSIONS AND COMMENT

From the experiments described we think it justifiable to conclude that the measuring of the reflex irritability of the eye, i. e., of the minimum reflexible, of a child in its first year of life can be employed as a means of deciding whether that child has an adequate vitamin A content.

If one looks at the experiments from a practical therapeutic point of view, they suggest that the diets poor in fat which are usually employed for infants may, if administered for a comparatively long period, bring about a deficiency in the vitamin A content without the child's presenting any clinical symptom other than a reduction in the reflex irritability to light. This is the first symptom of hypovitaminosis A which can be detected, and it can be detected long before the normal increase in weight or the normal growth in height of the child is impaired. A child who suffers from diarrhea is less able to utilize the small quantities of vitamin A contained in buttermilk, half skimmed milk and similar foods poor in fat.

We noticed that when dyspepsia is cured in some cases as little as from 0.1 to 0.4 per cent of fat in the diet is sufficient to bring about normal reflex irritability to light.

As to the diet minus animal fat, one should keep in mind that it is not entirely devoid of vitamin A, for both buttermilk and potatoes contain small quantities and even the so-called vegetable margarine sometimes contains whale fat.

With the form of diet minus animal fat which was employed in our experiments, the results tend to show that about six weeks elapses before the vitamin A content of the organism is exhausted and the reduction of the minimum reflexible becomes manifest. However, individual differences assert themselves.

Our results show that in many cases even a liberal supply of carrots is not always sufficient to meet the vitamin A requirements of the organism, for even great quantities of carrot juice and mashed carrots frequently proved insufficient to restore or bring about the normal minimum reflexible. Thus, the effect of carrots as a source of the production of vitamin A is inconstant.

As the diet minus animal fat is no doubt in some cases the best means available of causing the symptoms to disappear, care should be taken that spinach forms a part of this diet. As the majority of older children do not like spinach, the use of a preparation of dried spinach, the effect of which was unmistakable in all our experiments, is practicable regardless of the slight vitamin A content of the preparation.

Our results indicate further that young infants are unable to store a large reserve content of vitamin A. A water diet of no more than

twenty-four hours' duration frequently decreases the content so that the minimum reflexible is reduced.

For the treatment of diarrhea in infancy the inanition diet is the most important therapeutic measure whether the water diet is partial or complete and whether barley water, water gruel or rice water is used.

According to our experiments, it must be kept in mind that the child on a water diet incurs an acute deficiency in the vitamin A content. This deficiency is fairly rapidly cured, i. e., in from three to eight days, if the after-treatment consists of a diet of ordinary cow's milk mixture; it is still more rapidly cured if the child receives mother's milk. However, if the dyspeptic condition renders it necessary that the after-treatment consist of the administration of buttermilk, skimmed milk or children's food, the deficiency may persist for a longer period.

The inference is that if treatment by inanition must be carried out because of the particular symptoms and has to be followed, as is often the case, by a diet initially poor in fat but gradually containing more fat, it is best to administer vitamin A in a form which will agree with the child at that stage of the disease.

Our experiments, moreover, indicate that if a child has undergone a protracted preliminary treatment (for about six weeks) consisting of a diet poor in fat, such as the diet minus animal fat, and because of diarrhea receives a water diet for twenty-four or forty-eight hours, the vitamin A content becomes fairly exhausted and the requirements must be met by the administration of an extra supply of vitamin A. In one of our experiments, which was not included in this series, the prexerotic stage, with a minimum reflexible of 4.25, appeared without our having had any suspicion that it could develop so rapidly. It is natural to presume that this rapid development is peculiar to the very young, rapidly growing person, whose metabolism in many ways is characterized by great lability and whose vigorous growth requires an excessive consumption of vitamin A.

With the help of the colorimetric method, Toverud and Ender[4] recently observed that the livers of a series of dead new-born and premature children contained very little vitamin A, and they brought this observation into causal relation with the fact that the antepartum diet of the mother had been deficient in vitamin A. It should, however, be mentioned that nature itself tries to compensate for this deficiency by means of the colostrum, which is particularly rich in vitamins and, owing to its high calory content, is an extremely important factor of nutrition for the new-born infant.

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4. Toverud, K. U., and Ender, F.: Norsk mag. f. lægevidensk. **96**:947 (Sept.) 1935.

The efficiency in storage increases with age, and our experiments substantiate what Debré and Busson [2] suggested in their works, namely, that when the child passes from the monotonous milk diet to a mixed vegetable diet, the fixation of the vitamin A content increases.

That an isolated dose of a preparation of spinach administered to a child with latent hypovitaminosis A is able to prevent a reduction in the minimum reflexible for about a fortnight suggests that the vegetable supplement is not only speedily resorbed by, but also slowly excreted from, the organism.

The spinach preparation must have a special efficiency in supplying vitamin A from its carotene.

These experiments confirm the wisdom of the modern tendency toward early administration to the normal child of a mixed diet rich in vegetables, as contrasted with the former tendency toward administration of great quantities of milk,[5] which in other ways may even have a deleterious influence (e. g., in producing anemia or dystrophia).

Long before the existence of vitamin A was known, Czerny and Keller advocated a vegetable diet. On the other hand, it was not known that potatoes and carrots are not always sufficient.

If one looks at these experiments from the point of view of the medicaments used, one may say that the halibut liver oil preparation and the spinach preparation are both excellent and effective sources of vitamin A when they are administered in the dose generally indicated. Both the prophylactic use and the therapeutic use of the two preparations seem to be suitable for young infants.

The halibut liver oil preparation may be used in cases in which it seems desirable to supplement the effect of vitamin A with the effect of vitamin D. The spinach preparation may be used in cases in which it seems desirable to supplement the effect of vitamin A with the effects of vitamins B and C or in cases in which the patient is allergic to animal fats.

Finally, if one looks at the experiments from a theoretical point of view, it is evident that the carotene contained in carrots has not the same effect as the carotene contained in spinach. In cases in which even liberal doses of the carotene contained in carrots, 100 Gm. of which is calculated to contain 2,000 international (U. S. P.) units of vitamin A, produced no effect, a dose of from 100 to 200 units of vitamin A in the form of the spinach preparation produced an immediate effect. The inefficiency of the carrots was not affected by their being of the summer or of the winter crop.

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5. Friderichsen, C.: Kostformer i barnealderen, in Faber and Norgaard: Haandbog i diætetik, Copenhagen, 1933, p. 265.

The carotene contained in the aforementioned products consists chiefly of beta carotene, and the same chemical form is found in both. However, not all animals are able to form vitamin A from carotene. While to form this factor is normal for herbivorous animals, carnivorous animals cannot form vitamin A from green plants but do form it from meat. Carnivorous and omnivorous animals have but a small vitamin A content in the liver, in contrast to rats, in which 95 per cent of the entire vitamin A content is deposited in the liver.

Whereas mammals and fish which subsist chiefly on plants are always able to form vitamin A from carotene, Euler and Euler did not observe this transformation in the fish of prey Cobius niger after the administration of carotene, but they found the nontransformed carotene stored in the liver.

As yet too little is known about these relations in human beings because the methods hitherto employed have been too unreliable and because clinical experiments are difficult to interpret. Moreover, individual and constitutional factors assert themselves. It seems, at any rate after our experiments, that a human infant does not always react like a rat. With regard to the therapy, one must therefore take care not to jump at conclusions from animal experiments alone.

At any rate, Wieland,[6] under the heading, "Versagen des Karotins?" reported a case in which the findings are parallel with ours. After a troublesome dyspepsia during weaning, a child aged 2 weeks received skimmed mother's milk for ten days, and typical keratomalacia developed. The administration of carotene in a preparation which had a typical effect on rats did not improve the condition. Not till the child had received milk and cod liver oil did improvement ensue.

The mode of action of carotene in the human organism is not yet clear, and the results of the experiments which we here record tend to indicate a difference of action which cannot be elucidated by animal experiments alone.

We have commenced a series of clinical experiments with pure carotene containing 5,000 international (U. S. P.) units of vitamin A per gram, partly by means of the same method and partly by means of other methods, in order to examine the metabolism of the carotene itself. While this preparation had a marked effect in the experiments with rats we have not succeeded—by means of doses of from 500 to 600 international (U. S. P.) units—in obtaining any effect on the reflex irritability of the eye to light in the course of one hour, while a single dose of 100 international (U. S. P.) units of vitamin A in the form of the spinach preparation had a typical effect in the course of one-half hour in the same children. This further confirmed the

6. Wieland, E.: München. med. Wchnschr. **80**:1389, 1933; **87**:777, 1934.

surprising effect of the spinach preparation observed by us, and for the time being we must be content with ascertaining this as a fact and letting the explanation wait until continued investigations have gone to the bottom of the problem.

SUMMARY

1. A water diet of from twenty-four to forty-eight hours' duration brings about a gradual depletion of the vitamin A content, as measured by means of the reflex irritability of the eye to light (minimum reflexible), in the child's organism. This depletion is observed most distinctly in the infant who has been given milk only. The infant is unable to accumulate a large reserve of vitamin A from the milk alone, in contrast to the older child, who gets an abundant supply of vegetables in addition to the milk.

2. Vegetables bring about a better fixation of the vitamin A content of the organism, the water diet only reducing the minimum reflexible to a slight extent in the child who receives a mixed diet.

3. A number of the diets poor in fat which are generally used for infants may, when administered for a longer period, cause a vitamin A deficiency. This is true of the buttermilk diet and the diet minus animal fat and to a certain extent of the protein milk and the infants' food diet also.

4. Despite their great content of carotene, mashed carrots and carrot juice are not always able to prevent latent avitaminosis A. The transformation to vitamin A or its resorption must somehow have been impeded.

5. In contradistinction, the preparation of spinach (dried spinach) showed a rapid and more stable effect despite the smallness of the doses when measured in international (U. S. P.) units of vitamin A.

6. The clinical experiments showed that the process in the child is not fully parallel with that observed in animal experiments, since the carotene—administered in various forms—did not act on the irritability to light within half an hour in the doses in which one would expect it to from the animal experiments.

INGESTION OF VITAMINS A, B, C AND D AND POLIOMYELITIS

JOHN A. TOOMEY, M.D.
CLEVELAND

Some investigators have expressed the opinion that protection against poliomyelitis is a maturation phenomenon.[1] Others have stated the belief that protection bears some relation to the physical make-up of the human being.[2] Some of the histories of cases of poliomyelitis that I have studied suggested a correlation between the lack of certain vitamins and resistance to the disease.[3] It was decided that before experimentation was done with diets deficient in vitamins it would be wise to determine if the feeding of large amounts of vitamins would have any effect on protection.

EXPERIMENTS

EXPERIMENT 1.—In September 1933, ten Macacus rhesus monkeys were obtained soon after they had been weaned. Their weights ranged from 900 to 1,020 Gm., and according to the weight tables of Schultz,[4] the monkeys must have averaged approximately from 6 to 7 months of age. From October 4 to 7, five of the animals were given 5 drops of 0.3 per cent carotene in oil (10 drops of which is equivalent to 1,000 U. S. P. units of vitamin A); from October 8 to 13, 10 drops; from October 14 to 19, 15 drops, and from October 20 to December 7, 20 drops. The animals were fed an increased amount of milk combined with raw eggs beginning on Jan. 26, 1934. They received an adequate diet of bananas, apples, oranges, etc. (vitamin C). Daily for ninety days before injection of virus they were also fed 1 drachm (4 Gm.) of powdered Embo and ½ drachm (2 Gm.) of brewer's yeast (vitamin B complex). There was no apparent discoloration of the mucous membrane, even though each animal had received more than 750,000 U. S. P. units of vitamin A. The fur of the animals was sleek and glossy, and they were active.

From the Department of Pediatrics, Western Reserve University School of Medicine, and the Division of Contagious Diseases, City Hospital, and aided in part by grants received from the S. M. A. Corporation and the Cleveland Foundation.

1. Poliomyelitis: A Survey Made Possible by a Grant from the International Committee for the Study of Infantile Paralysis, Baltimore, Williams & Wilkins Company, 1932, p. 452.

2. Draper, G.: Acute Poliomyelitis, Philadelphia, P. Blakiston's Son & Co., 1917; Am. J. M. Sc. **184**:111, 1932.

3. Toomey, John A.: A Predisposing Factor in Poliomyelitis, to be published.

4. Schultz, Adolph H.: Growth and Development, in Hartman, C. G., and Straus, W. L., Jr.: Anatomy of the Rhesus Monkey (Macaca Mulatta), Baltimore, Williams & Wilkins Company, 1933, chap. 2.

On December 8 each of these five animals and also five controls (group 2) were given intracerebral injections of 0.05 cc. of a 1 per cent suspension of poliomyelitis virus. Nine of the animals had complete quadriplegia on the sixth day after the injection. The remaining animal had complete quadriplegia on the ninth day.

Autopsies showed no signs of local infection either in the gastro-intestinal tract or in the lungs. The lungs were a peculiar, light cream-tan color in three of the five specimens from monkeys that had received carotene. There was hemorrhagic pneumonia in one animal, dilatation and hyperemia of the intestines in all of them and a large paralyzed bladder in four of the group that had been fed carotene.

The ingestion by monkeys of massive doses of vitamins A, B and C did not in any way aid them to ward off the effects of intracerebral injections of poliomyelitis virus.

EXPERIMENT 2.—While the animals were being prepared another experiment was in progress. On March 16, 1934, ten Macacus rhesus monkeys were isolated for experimentation. Five (group 3) were fed a complete diet with an excess of vitamins A, B and C and in addition were given 2 drops of viosterol daily until May 13. Five animals (group 4) were fed the routine laboratory diet. Two died during the period of preparation. The eight animals that remained were given intracerebral injections of 0.5 cc. of a 1 per cent suspension of poliomyelitis virus, and quadriplegia developed in all eight. This experiment would indicate that the ingestion of massive doses of vitamins A, B, C and D failed to protect monkeys that subsequently received intracerebral injections of virus.

EXPERIMENT 3.—Since I believe that the portal of entry for poliomyelitis is the gastro-intestinal tract,[5] I decided to feed vitamins A, B, C and D to monkeys and then see what effect virus given by way of the gastro-intestinal tract would have on them.

Five animals (group 5) were fed as were those in group 3, receiving all four vitamins. Two drops of viosterol was given daily from May 1, when preparation began. Five animals (group 6) were given vitamins A, B and C, but not D. Beginning on July 8 of the same year all animals received virus, which was injected into the lumen of the intestine, as previously described.[6] None of the animals protected with vitamin D contracted the disease. In all five animals of group 6 not protected with vitamin D the disease developed, and one of them died of quadriplegia (table 1). Animal 1-460A which was given an intracerebral injection of 0.5 cc. of a 10 per cent suspension of the lumbar cord from animal 1-460 had typical quadriplegia seven days after the injection.

It can be seen that the ingestion of large doses of vitamins A, B and C did not protect the animals receiving them. On the other hand, the animals that were given vitamins A, B, C and D were protected from the effect of the virus when it was introduced by way of the gastro-intestinal tract.

EXPERIMENT 4.—Would the lack of vitamin D in the diet of young Macacus rhesus monkeys decrease their resistance to poliomyelitis virus introduced by way of the gastro-intestinal tract? Young monkeys were fed the diet recommended

5. Toomey, John A.: The Gastrointestinal Portal of Entry in Poliomyelitis, J. Pediat. **8**:664, 1936.

6. Toomey, John A.: Spread of Poliomyelitis Virus from the Gastrointestinal Tract, Proc. Soc. Exper. Biol. & Med. **31**:680, 1934.

by Gerstenberger to produce rickets.[7] Preparation extended from Dec. 5, 1935, to April 7, 1936, and at various intervals after that two animals at a time were operated on and given subserosal injections of virus. This method of injection provided a more severe testing of the animals' resistance than would the introduction of the virus between clamps. It was deemed quite possible that when this

TABLE 1.—*Protocol for Experiment 3*

Date	Dosage and Concentration of Virus Suspension	Controls Not Protected with Vitamin D but Protected with Vitamins A, B and C		Animals Protected with Vitamins A, B, C and D	
		Animal Number	Result	Animal Number	Result
7/ 8	140 cc. of 1.5%	1-466	Quadriplegia; died 7/11	2-466	No effect
7/13	135 cc. of 1%	3-462	Tremor; paresis of left leg and foot; slight weakness of right leg	4-467	No effect
7/16	150 cc. of 2%	5-463	Paresis of right foot and both legs	6-468	No effect
7/17	150 cc. of 2%	7-464	Furred and inactive	8-469	No effect
7/22	150 cc. of 2%	9-465	Paresis of right foot and leg	10-470	No effect

TABLE 2.—*Protocol for Experiment 4*

Date	Dose and Concentration of Virus Suspension	Controls Not Protected with Vitamin D but Protected with Vitamins A, B and C		Animals Protected with Vitamins A, B, C and D	
		Animal Number	Result	Animal Number	Result
4/ 7	35 cc. of 1%	805*	Typical quadriplegia; died 4/19	681	Weakness of left foot and leg
4/22	50 cc. of 1%	800	Paresis of both feet and left leg	683	No evidence of disease
4/22	50 cc. of 1%	803*	Bulbar type; died 5/3	685	Slight weakness of left foot
5/ 9	50 cc. of 1%	694*	Typical quadriplegia; died 5/29	684	No evidence of disease
5/19	50 cc. of 1%	695*	Typical quadriplegia; died 5/31	679	No evidence of disease
5/26	50 cc. of 5%	802	Typical quadriplegia; died 6/3	675	No evidence of disease
5/26	50 cc. of 5%	690	Both legs paralyzed completely	676	No evidence of disease; died 5/27 of acute gastric (operative death) dilatations
6/22	50 cc. of 5%	691*	Died on operating table; death due to anesthetic	866	No evidence of disease
6/22	50 cc. of 5%	689*	Typical bulbar involvement; died 6/29	678	Typical bulbar involvement; died 7/3
7/ 3	50 cc. of 5%	696*	Typical bulbar and spinal involvement; died 7/9	872	No evidence of disease

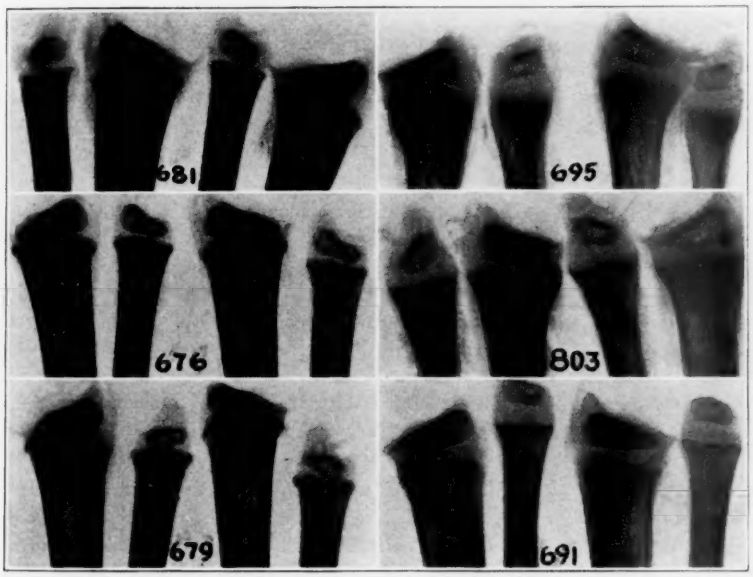
* Had definite beading of the ribs.

method was used mild poliomyelitis might be produced even in the protected animals. Even so, the object of this experiment was to determine distinctive and unquestionable differences between animals which had received vitamin D and those which had not.

7. Gerstenberger, H. J.: Rickets in Rhesus Macaques, to be published.

To what extent rickets developed in the animals deprived of vitamin D is unknown, since no chemical studies of the blood or histologic studies were made. However, in some of the animals beading of the ribs developed, which under the conditions of this experiment would justify the tentative diagnosis of clinical rickets, and there were obvious abnormalities in the wrists, as can be seen from the sample roentgenograms here reproduced.

Ten animals (group 7) were protected with vitamins A, B, C and D. Ten animals (group 8) were protected with vitamins A, B and C only. One of the animals in group 7 died on the operating table, and one of those in group 8 died the next morning as a result of the operation. Of the remaining nine animals in group 8 all contracted typical poliomyelitis, and seven of them died. In group 7, six of the nine animals gave no evidence of disease, two had weakness of the legs and only one, which had typical bulbar poliomyelitis, died



Roentgenograms showing bones of the wrists of monkeys. Animals 681, 676 and 679 were fed a diet in which were all the vitamins, including vitamin D. Animals 695, 803 and 691 were given the Gerstenberger rickets-producing diet.

Thus, regardless of the severity of the operation performed to inject the virus, it would seem from this experiment that the omission of vitamin D from the diet made the animals more susceptible to poliomyelitis when the virus was given by way of the gastro-intestinal tract.

EXPERIMENT 5.—Because heterolateral paresis usually can be produced immediately when enteric toxins are added to virus and injected intracerebrally,[8] plans

8. Toomey, J. A.: Accelerated Production of Poliomyelitis, Proc. Soc. Exper. Biol. & Med. **31**:1015, 1934.

were made to deprive monkeys of vitamin D and to give them large injections of vaccines made from organisms of the colon groups and their toxins. Five young monkeys were isolated on October 8, 1933, kept out of the sunlight and fed the routine diet plus large amounts of vitamins A, B and C but no vitamin D. The animals were given subcutaneous injections of various amounts of vaccine and toxin throughout a period of four months, as previously described.[9] Two animals died during the course of preparation. Three newly purchased monkeys were used as controls. The other three animals were given injections of virus subserosally or between clamps on March 1, nearly six months after preparation had been begun. The three recently acquired, untreated animals (group 9) showed mild monoparesis or paraparesis, from which they soon recovered. The three animals which received injections of colon bacillus toxin (group 10) succumbed to typical poliomyelitis, all within twelve days afterward.

Specimens from the lumbar portions of the cords of the three animals that died were tested for the presence of virus by giving intracerebral injections of 0.5 cc. of a 10 per cent suspension, prepared from the specimens, to three normal animals. All three animals contracted poliomyelitis, thus demonstrating the fact that the virus was present in the cords of the animals that died after it had been introduced by way of the gastro-intestinal tract. It also was seen that monkeys deprived of vitamin D were made more susceptible to poliomyelitis virus by being previously given injections of colon organisms and their toxic products.

EXPERIMENT 6.—The next experiment was planned to avoid the drastic procedures of clamping the intestine or subserosal injection—methods employed by me as a routine to introduce the virus. Three animals deprived of vitamin D (group 11) but fed large quantities of vitamins A, B and C were given injections of colon bacillus toxin vaccine during a period of two months. They were then operated on, and from 150 cc. to 200 cc. of a 10 per cent suspension of virus was introduced directly into the intestine without any mechanical injury. All three of the animals contracted the disease, two having quadriplegia and one, complete paraplegia. In none of the three controls (group 12) that had received vitamin D did the disease develop.

Intracerebral injections of 0.5 cc. of a 10 per cent suspension of the lumbar portions of the cords of both the animals that died and the animal that had paraplegia were given to three normal animals. All three contracted poliomyelitis. Thus it is seen that animals can be so prepared that by simply putting the virus into the gastro-intestinal tract the disease is produced.

COMMENT

One would hesitate to maintain that rickets is the sole clinical entity that conditions the gastro-intestinal tracts of monkeys to the point where they contract poliomyelitis more easily, but it is clear that the lack of vitamin D can bring about such a result in the animals. The virus naturally absorbed by the naked gray fibers or axis-cylinders of medullated nerves in the normal animal may be prevented from spread-

9. Toomey, J. A.: Effect of Poliomyelitis Virus in Baby Monkeys Previously Given Paratyphoid Colon Filtrate and Vaccine, Proc. Soc. Exper. Biol. & Med. **32**:862, 1935.

ing to the cord by the insulated myelinated nerve sheath. Thus immunity might depend on the state of the myelin of the sympathetic and parasympathetic nerves at the moment. Giving vitamin D may be one way of improving the state of this absorbing or insulating substance, and it is a plausible supposition that the lack of this vitamin in infancy may leave a poorly insulated myelin sheath which can be affected by various conditions more easily than are the nerves of subjects who have had adequate doses of vitamin D.

It is paradoxical that, though the lack of vitamin D makes monkeys more susceptible to poliomyelitis, the rise in the morbidity of the disease occurs at that time of year when human beings theoretically should receive plenty of the antirachitic factor from the summer sun.

I recently found that the blood serum of eight rachitic children taken during the active stage of the disease contained no agglutinins against organisms of the enteric group, and since the agglutinin titer against enteric organisms of blood serum taken from animals in the prostate stage of poliomyelitis is practically nil,[10] a possible connection is thought to exist between the lack of vitamin D and the lack of agglutinins against enteric organisms. Another point noticed in regard to the eight children was that when the roentgenographic evidence and the readings for calcium and phosphorus in the blood serum had become normal, agglutinins against enteric organisms had not yet appeared, their production lagging behind the other physical and biochemical findings of recovery. More cases of rickets have to be studied before any definite conclusions can be drawn. However, there may be a loss of agglutinins against enteric organisms on account of the lack of vitamin D, and there may be a lag in the production of agglutinins long after exposure to sunlight of the human being who lacked vitamin D. Since the lack of agglutinins against enteric organisms makes monkeys more susceptible to poliomyelitis when the virus is given by way of the gastrointestinal tract and since this susceptibility is further enhanced by subcutaneous injections of enteric organisms and their toxins, it is not illogical to suspect a connection between the loss of agglutinins, the susceptibility to the disease and the lack of vitamin D.

In connection with this discussion of vitamin D, it may be interesting to note that I have found that the virulence of virus preparations is decreased after exposure to ultraviolet radiation.[11]

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10. Toomey, J. A.: Changes in Titers of Agglutinins for Enteric Organisms in the Blood Serum in Poliomyelitis, J. Infect. Dis. **54**:74, 1934.

11. Toomey, John A.: Action of Ultraviolet Ray on Poliomyelitis Virus, to be published.

CONCLUSION

On the whole, it is fair to conclude from these experiments (1) that the ingestion of vitamin D protects Macacus rhesus monkeys from poliomyelitis when the virus is subsequently introduced by way of the gastro-intestinal tract; (2) that the lack of vitamin D in the routine diet makes the animal more susceptible to the disease when the virus is given by way of the gastro-intestinal tract, and (3) that animals may be given such diets and so prepared that poliomyelitis can later be produced merely by introducing the virus into the gastro-intestinal tract.

LICHEN URTICATUS (PAPULAR URTICARIA)

TREATMENT WITH PARATHYROID EXTRACT; THEORETICAL CONSIDERATION OF THE ETIOLOGY

DONALD M. PILLSBURY, M.D.
AND
THOMAS H. STERNBERG, M.D.
PHILADELPHIA

Lichen urticatus constitutes a large proportion of the cutaneous diseases encountered in children. At the Children's Hospital of Philadelphia approximately one fourth of the patients admitted to the dermatologic clinic during the spring and summer months are suffering from this disease. We have been consistently impressed with the ineffectiveness of most of the recommended methods of treatment, with the notable exception of parathyroid extract, first suggested by Cornbleet,[1] which has thus far received little attention in the literature. We are therefore presenting our results in a series of patients treated in this manner, with a series of control patients treated by other means. Certain theoretical considerations as to the etiology of the disease have occurred to us from our experience and from a survey of the literature.

Parathyroid extract has attained a minor place in dermatologic therapy in recent years. Cornbleet [1] in 1929 reported the successful treatment of twenty-one patients with lichen urticatus with parathyroid extract administered subcutaneously in conjunction with calcium lactate administered orally. A detailed report of three of his cases indicated that the itching was relieved within a week and that it was rarely necessary to continue treatment for more than six weeks. The addition of calcium lactate administered orally in massive doses was found to be more effective than the extract alone. Thus far there has been no published confirmation of Cornbleet's work. Tate [2] mentioned the use of parathyroid extract in the treatment of this disease but presented no evidence concerning it. Sellei [3] highly recommended the use of parathyroid extract in combination with other therapeutic measures in the

From the Department of Dermatology and Syphilology of the School of Medicine of the University of Pennsylvania, John H. Stokes, M.D., director, and the Dermatology and Sigma Clinic of the Children's Hospital.

1. Cornbleet, T.: The Use of Parathyroid Extract in Lichen Urticatus, Arch. Dermat. & Syph. **19**:281 (Feb.) 1929.

2. Tate, B. C.: Urticaria Papulosa, Arch. Dis. Childhood **10**:27 (Feb.) 1935.

3. Sellei, J.: The Treatment of Chronic Alimentary Urticaria, Quincke's Edema and Eczema Dyshidrosis with Parathyroid Hormone, Calcium and Therapeutic Diet, Dermat. Wchnschr. **93**:1963, 1931.

treatment of chronic alimentary urticaria and angioneurotic edema. In another publication [4] he stated his belief that this substance when given two or three times weekly helps to shorten the course of dyshidrosis and to lessen the frequency of relapse. Richter and Herzfeld [5] have reported favorably on the value of parathyroid extract in the treatment of urticaria, rosacea, neurodermatitis and reactions to iodides and arsenic taken internally. Lindenfeld [6] has reported the successful treatment of kraurosis vulvae with a parathyroid preparation.

Other successful methods of treating lichen urticatus have been reported by various investigators. Hallam [7] originally observed an immediate cessation of the eruption on confinement of the patient to a hospital, whether other therapy was instituted or not, with a rapid recurrence of the lesions on the patient's return home. This observation was later confirmed by Kinnear,[8] Gordon,[9] Tate [2] and others. Bray [10] obtained good results by the elimination of hog products and fried foods from the diet, the administration of pepsin and hydrochloric acid internally and the prevention of overheating. Gordon [9] reported favorably on the use of ammonium bromide in conjunction with phenolated lotion of calamine locally.

It is generally agreed, however, that in most cases therapy has offered only varying degrees of temporary subjective or objective relief, the usual course being characterized by chronicity and frequent exacerbations, with complete remission in the fall of the year lasting through the winter.

CLINICAL FEATURES

Lichen urticatus, or papular urticaria, is a clearcut syndrome which ordinarily offers no difficulty in diagnosis. Little can be added to Bateman's [11] original description of the disease, published in 1813. In discussing various lichenoid dermatoses, Bateman stated that he had observed

> one form, which is so uniform in its character, as to be entitled to be noticed here. It may be called lichen urticatus; as its first appearance is in irregular, inflamed

4. Sellei, J.: Parathyroid Therapy as an Aid in Dyshidrosis, Urol. & Cutan. Rev. **36**:384, 1932.

5. Richter, W., and Herzfeld, E.: Parathyroid Therapy in Dermatology, München. med. Wchnschr. **79**:1650, 1932.

6. Lindenfeld, F.: Kraurosis of Vulva Successfully Treated with a Parathyroid Preparation, Gyógyászat **73**:639, 1933.

7. Hallam, R.: Further Observations on the Aetiology of Papular Urticaria, Brit. J. Dermat. **44**:117, 1932.

8. Kinnear, J.: Urticaria Papulosa with Notes of Fourteen Cases with Unusual History, Brit. J. Dermat. **45**:65, 1933.

9. Gordon, H.: Lichen Urticatus, Lancet **2**:126, 1933.

10. Bray, G. W.: Lichen Urticatus, Brit. J. Child. Dis. **30**:180, 1933.

11. Bateman, Thomas: A Practical Synopsis of Cutaneous Diseases, ed. 3, London, Longman, Hurst, Rees, Orme and Brown, 1814.

wheals, so closely resembling the spots excited by the bites of bugs or gnats, as almost to deceive the observer. The inflammation, however, subsides in a day or two, leaving small, elevated, itching papulae. While the first wheals are thus terminating, new ones continue to appear in succession, until the whole body and limbs are spotted with papulae, which become here and there confluent, in small patches. The eruption is peculiar to children; it commences, in some cases, soon after birth, and sometimes later, and continues with great obstinacy for many months. Both the wheals and the papulae are accompanied with intense itching, which is exceedingly severe in the night, occasioning an almost total interruption of sleep, and considerable loss of flesh.

The localization of the eruption in our cases has been a striking feature. The areas of predilection in the order of most marked involvement are the extensor surface of the forearms, the anterior surface of the legs, the face, the outer surface of the upper part of the arms and the back. The secondary changes which might be expected in any chronic highly pruritic eruption, namely, excoriation, lichenification and various pyodermas, were evident in many of our cases. The initial transitory wheal was frequently topped by a small vesicle the size of a pinpoint. In cases of severe involvement a few scattered lesions might be seen on the flexor surfaces of the arms and on the abdomen. The most frequently considered condition in the differential diagnosis was scabies, and when confusion seemed possible the patient was given a therapeutic test with sulfur ointment.

REPORT OF CASES

A total of sixty patients with lichen urticatus are included in this series. Forty-three were Negroes, and thirty-three were males, all of them coming from families of poor financial condition. The nutritional status of the patients as a whole was good.

The ages of the patients at the time of the onset of the first attack varied from a few weeks to 12 years, 37 per cent of the patients being less than 1 year of age, 66 per cent being less than 2 years and 83 per cent being less than 3 years. Many of these patients were suffering a fourth or fifth seasonal attack when first admitted to the clinic.

The seasonal incidence of the disease is strikingly illustrated in table 1. In 85 per cent of the patients the eruption first appeared during the months from April to August, inclusive. May and June contributed the largest number, with thirteen each, and July was next, with twelve. This observation is confirmed by all investigators.

METHODS OF THERAPY

All but eleven of the patients received some form of local treatment. The lotions consisted of the following ingredients in various combinations: phenol, zinc oxide, boric acid, calamine, salicylic acid, coal tar solution, solution of calcium hydroxide and olive oil. Other preparations used were 3 per cent ammoniated mercury ointment, 5 per cent sulfur ointment, a zinc paste, 3 per cent sulfonated bitumen in zinc oxide ointment and from 3 to 6 per cent crude coal tar ointment.

Calcium lactate, calcium gluconate or dicalcium hydrogen phosphate was given internally to each patient, usually in milk, the dose varying from 3 to 8 Gm.

daily, depending on the size and age of the patient. A number of patients were receiving or were given cod liver oil in adequate doses.

Parathyroid extract was given subcutaneously to thirty-four patients at weekly or biweekly intervals, depending on the severity of the process. The optimal dose for infants was considered to be from 10 to 15 units,[12] while the older children received from 20 to 25 units in each injection. None of the symptoms of an overdose, such as loss of appetite, dulness, loss of initiative, somnolence, vomiting, decrease in the general body tone or impairment of the circulation, was observed.

The effectiveness of parathyroid extract in the treatment of lichen urticatus is well shown in table 2, the end-results being good or excellent in 85 per cent

TABLE 1.—*Month of Onset of Eruption*

Month	Cases
January	1
February	3
March	4
April	6
May	13
June	13
July	12
August	7
September	1
October	0
November	0
December	0

TABLE 2.—*Results of Therapy*

	Parathyroid Extract; Topical Applications; Calcium Internally		Topical Applications; Calcium Internally	
Therapeutic Result	No. of Cases	Percentage	No. of Cases	Percentage
Excellent *	14	41.2	2	7.7
Good †	15	44.1	8	30.8
Poor ‡	2	5.9	10	38.4
Unknown §	3	8.8	6	23.1
Total	34		26	

* Complete involution of eruption within four weeks, with no recurrences.
† Protracted course of from one to five months but held at a minimum by treatment.
‡ Therapy of little or no benefit.
§ Discontinued treatment with result unknown.

of the patients, as compared with 38 per cent in the control group. In many of the patients the action of the drug was striking, the itching being relieved almost immediately and the scratch papules involuting in a few days. In other cases it seemed that the interval between injections was excessive, as itching and new cutaneous lesions appeared one or two days before the time for the next treatment. In the cases of more severe involvement it was necessary to give the injections biweekly. Eleven of the thirty-four patients in the group treated with parathyroid extract were given no local medication. The response was slightly inferior to that

12. On the basis of the doses used previous to 1935 this would be 2 or 3 units. A portion of the parathyroid extract used in this study was furnished by Eli Lilly & Co.

of all the patients treated with parathyroid, because of the longer time required for the secondary cutaneous complications, such as scratch dermatitis and infection, to subside.

Eleven of the sixty patients were studied for sensitivity by means of multiple scratch tests with the common antigens. All of these patients reacted to one or more of the allergens, but in no case was there any improvement after the removal of the reacting substances from the diet or environment. This observation is in agreement with several recent reports indicating that allergic studies are of little value in papular urticaria.

Knowledge concerning the action of parathyroid extract may be summarized as follows: Schmidt and Greenberg,[13] in a recent review of calcium, magnesium and phosphorus metabolism, discussed fully the response of the animal organism to the subcutaneous administration of parathyroid extract. There is an increase in the calcium content of the blood, which reaches its maximum in from twelve to eighteen hours. A small rise in the potassium and magnesium levels of the blood serum also is noted, the maximum rise of the magnesium level occurring within from two to four hours and returning to normal long before the peak of the rise of the calcium level is reached. The increase of the calcium content of the serum is mostly at the expense of the stores in the bones. The inorganic phosphate content of the blood is temporarily decreased after the injection. Greenberg and Tufts [14] found that when an increase of only about 2 mg. per hundred cubic centimeters is produced in the content of serum calcium by parathyroid extract, the rise occurs almost wholly in the diffusible fraction. When the rise is greater than this, it is divided equally between the diffusible and the nondiffusible fraction. Gilligan and his associates [15] found that the calcium concentration of edema fluid increases after the administration of parathyroid extract and that this increase is quantitatively similar to the increase in the calcium content of the serum. This observation demonstrates further that the fraction of calcium mobilized in the plasma by the injection of small doses of parathyroid extract is mainly if not entirely diffusible.

A REVIEW OF CURRENT ETIOLOGIC CONCEPTIONS

Most of the views presented on the etiology of lichen urticatus have been based on the assumption that the causative agent is an unknown

13. Schmidt, Carl L. A., and Greenberg, David M.: Occurrence, Transport and Regulation of Calcium, Magnesium and Phosphorus in the Animal Organism, Physiol. Rev. **15**:297, 1935.

14. Greenberg, David M., and Tufts, E. V.: The Formation of a Colloidal Form of Calcium Phosphate in the Blood Stream in Experimental Hypercalcemia, J. Biol. Chem. **105**:xxxii, 1934.

15. Gilligan, D. R.; Volk, M. C., and Altschulte, M. D.: Diffusibility of Plasma Calcium Following Parathormone Administration, J. Biol. Chem. **103**:745, 1933.

allergen or allergens. We believe that this assumption may be erroneous and that the evidence supporting it is meager or at least not susceptible of proof by present methods of allergic study, and although there have been a few reports of cures from the removal of allergens eliciting a positive reaction, the collected results obtained from these studies are insignificant. Engman and Wander [16] reported four cases of lichen urticatus in which the skin was tested with multiple antigens with negative results. Corson and his associates [17] reported on thirty-one patients, twenty-one of whom showed negative reactions to all skin tests. Of the ten who showed a positive reaction to the various antigens, only one was cured by elimination. Sidlick and Knowles [18] reported obtaining a cure or improvement in seven of twelve patients with removal from the diet of food antigens causing positive reactions. Walzer and Grolnick [19] have recently published a most thoroughgoing study of the relation of papular urticaria to allergy. They investigated forty-one patients (five of whom they said had prurigo mitis); seventeen gave a positive history of familial atopy and six had past or present manifestations of allergy. They noted positive reactions to various allergens in nine of their patients but six of these had a history or evidence of infantile eczema or asthma. They found that all the patients with an increased percentage of eosinophils had a personal or familial history of allergy. "Specific" treatment based on the results of the skin testing, i. e., by removal of the positively reacting substances from the patient's diet or environment, was of no value in papular urticaria or prurigo mitis. Walzer and Grolnick concluded that the positive reaction to the skin tests have no relation to papular urticaria but are part of the atopic state which the patients present and that skin testing is of no diagnostic or therapeutic value in papular urticaria. Hallam [7] stated as his conclusion that foods do not play a rôle in the etiology of the disease and that the condition is an allergic reaction to something in the patient's environment. He reported that the eruption cleared immediately after the patient's admittance to the hospital, although a study for possible antigens in the bedding and home surroundings was fruitless. Tate,[2] in an extended series of careful experimental studies,

16. Engman, M. F., and Wander, W. G.: The Application of Cutaneous Sensitization to Diseases of the Skin, Arch. Dermat. & Syph. **3**:223 (March) 1921.

17. Corson, E. F.; Perlman, H. H.; Waltz, A. D., and Ash, R.: Urticaria Papulosa: Clinical, Serologic and Chemical Investigation, Arch. Pediat. **48**:349, 1931.

18. Sidlick, D. M., and Knowles, F. C.: The Value of Cutaneous Sensitization Tests Employed in Eczema and Papular Urticaria of Childhood, Am. J. Dis. Child. **23**:316 (April) 1922.

19. Walzer, A., and Grolnick, M.: Urticaria Papulosa—Relation to Allergy, J. Allergy **5**:245, 1934.

noted that the room temperature in most hospital wards in London is usually below 68 F. and that a temperature at least this high is necessary for the production of fresh lesions. He concluded that the etiologic agent is an unknown antigen. More recently it has been agreed by most observers that lichen urticatus and urticaria are distinct syndromes and that, while the two conditions may occur in a patient simultaneously, this is uncommon, and the respective courses are independent. Only one of our patients had typical urticaria. Bray [10] stated his belief that hog products and such common foods as fish, eggs, potatoes, oats and chocolate are exciting factors and that fats are particularly involved.

Other etiologic views have been presented which are concerned only indirectly or not at all with allergy. Winnicott [20] has expressed the belief that lichen urticatus is a normal cutaneous phenomenon, an indication of excitement corresponding to the erection of erectile tissue, "in which the skin has become the battleground of a fight chiefly unconscious between an urge demanding gratification and a sense of guilt which threatens to deprive the child of an entire pleasure system." Gordon [9] stated that some cases represent "dermatologic neuroses" and that others are the result of overloading of the colon, food idiosyncrasy or any peripheral irritation. Hutchinson and Burnet have stated that flea bites are the commonest cause of the disease. Haxthausen [21] found that in Copenhagen there was an increase in the number of cases coincident with the period of ripening of the commoner fruits, but he was unable to prove any direct relationship. Wile [22] said he considered that the underlying factors are an irregular diet and a vasomotor disturbance of the skin as a result of toxins generated in the gastrointestinal tract, while such external influences as insect bites, fleas, bedbugs and scabies may be the exciting factors. Cole, in the discussion of a case of papular urticaria presented before the Cleveland Dermatological Society by Connor,[23] pointed out that no improvement had been noted until adequate doses of cod liver oil were given. La Rocco, discussing the same case, stated that in several cases of papular urticaria he had given vitamin D with more or less specific effect. It may be pointed out that in Connor's case improvement occurred while the patient was in the hospital and when the disease was normally at its

20. Winnicott, D. W.: Papular Urticaria and the Dynamics of Skin Sensation. Brit. J. Child. Dis. **31**:5, 1934.

21. Haxthausen, H.: Seasonal Influences on Various Diseases of the Skin, Bibliot. f. læger **147**:196, 1925.

22. Wile, Udo J.: The Urticaria of Infancy, Am. Med. **5**:42, 1910.

23. Connor, W. H.: Lichen Urticatus, Arch. Dermat. & Syph. **33**:557 (March) 1936.

lowest seasonal ebb. In our patients receiving adequate doses of cod liver oil we did not note any improvement which seemed particularly due to this factor. It must be remembered, however, that the effects of parathyroid extract and vitamin D are similar in one respect, namely, the increase in the calcium content of the serum, and if further observation confirms the finding that cod liver oil has a beneficial effect on the disease, the rôle of calcium metabolism in its etiology seems even more probable. Cantarow,[24] in a consideration of the principles of calcium therapy, pointed out that calcium metabolism may be influenced by parathyroid hormone, vitamins B, C and D, thyroxin, acid-base balance, renal function and the supply and degree of absorption of calcium and phosphorus. In comparing the effects of parathyroid extract and vitamin D, he stated that they act similarly only in increasing the calcium content of the serum and dissimilarly in that parathyroid extract decreases the phosphorus content, while vitamin D increases it; that parathyroid extract increases the elimination of calcium and phosphorus, while vitamin D causes retention, and that the increase in the calcium content noted with both is, in the case of vitamin D, due to an increased absorption from the intestine, while parathyroid extract has this effect through absorption of calcium from the bones and other tissues.

THEORETICAL CONSIDERATION OF THE ETIOLOGY

We believe that certain features of papular urticaria stand out prominently and that logical integration into a working hypothesis for further study is possible. The features which have impressed us particularly are (1) the incidence in infancy and early childhood, with disappearance of the eruption at or before puberty, (2) the marked seasonal incidence, (3) the demonstrable effects of an agent influencing calcium metabolism, namely, parathyroid extract, and (4) the demonstration that, at least by present methods of study, the disease is not due to a known allergen. It will be apparent that our consideration of this problem is probably overbalanced by our experience with parathyroid extract in the treatment of lichen urticatus. While it seems probable to us that some disturbance of calcium metabolism may be the underlying factor, we wish to point out that the effect of parathyroid extract should not be interpreted as necessarily affecting the basic etiologic factor directly. It may simply bring about a break in the complex and in the little understood chain of disturbances which has been initiated.

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24. Cantarow, A.: Fundamental Principles of Specific Calcium Therapy, Pennsylvania M. J. **37**:457, 1934.

Parathyroid extract probably acts through its effect on calcium metabolism by increasing the amount of the diffusible fraction in the blood. This action may be represented in the following formula, which is in part empirical:[13]

$$\frac{Na^{+} + K^{+} + OH^{-}}{CA^{++} + Mg^{++} + H^{+}}$$

An increase in the ions in the numerator leads to an increase in the irritability of the tissues; an increase in the ions of the denominator reduces it. While the total calcium content of the blood may remain the same, a reduced diffusible fraction results in hyperirritability of the nervous system and other tissues. Kallós and Kallós-Deffner[25] and others have presented evidence indicating that the efficacy of calcium is the result of a lessened permeability of the marginal layer of cells and a reduction of the irritability of the sympathetic nervous system.

Age Incidence.—No logical explanation of this factor is apparent. It has been shown that two substances may be isolated from the thymus gland, one of which lowers the calcium content of the serum and the other lowers the phosphate content of the serum,[26] and that the presence of these hormone-like substances is not limited to the thymus gland but is general in all lymphoid tissue, including the spleen. The peculiar susceptibility of the infant and of the young child to eczema has not been satisfactorily explained. While definite allergens may be demonstrated in some cases of eczema, any extended experiments with the disease impress one with the frequently disappointing results of such studies and with the fact that there remains a vital quantity *x* in eczema as well as in papular urticaria.

Seasonal Incidence.—Several factors may be contributory to this feature of papular urticaria, some of which have already been the subject of careful study. The work of Tate,[2] indicating that heat is a definite precipitating agent, has been mentioned. The possible influence of sunlight has been considered by several investigators, among them Sellei and Liebner,[27] who found that exposure of the patient to ultraviolet radiation at sites other than those involved by the disease precipitated a recrudescence of lesions at the sites previously involved but did not induce any lesions in the irradiated area. We are not prepared to state that light may not be a factor, but we do not believe it to be the principal one. The frequency with which the disease occurs

25. Kallós, P., and Kallós-Deffner, L.: Experimentelle Untersuchungen zur Calciumtherapie allergischer Zustände, Klin. Wchnschr. **14**:1247, 1935.

26. Nitschke, A.: Ueber die Zustandsform des Calciums im Serum, Biochem. Ztschr. **192**:123, 1928.

27. Sellei, J., and Liebner, E.: Ueber Prurigo aestivalis, Arch. f. Dermat. u. Syph. **152**:19, 1926.

in colored skin constitutes one argument, though not an irrefutable one, as witness the occurrence of a light-sensitive dermatosis, lupus erythematosus, in Negroes. We have noted no effect, beneficial or otherwise, in the few cases in which ultraviolet irradiation was employed. We know of no instance in which a person not already subject to the disease has had an attack precipitated by exposures to ultraviolet radiation. Theoretically, in view of the influence of sunlight on calcium metabolism, one might expect that it would have a beneficial effect.

It is well known that seasonal variations in the calcium-phosphorus ratio of the serum occur.[28] A further factor lies in the possible effect of ingestion of oxalate-containing leafy vegetables during the summer months. The large amount of oxalate which may be ingested in this manner has recently been pointed out,[29] and the formation of insoluble physiologically inert calcium oxalate in the intestinal tract or blood stream has undoubted possible significance. Another dietary factor, somewhat seasonal in character, may lie in a diminished ingestion of fats, which, according to Holt and Fales,[30] results in changes in the stool and in lessened absorption of calcium from the intestinal tract.

ACTION OF PARATHYROID EXTRACT

It seems probable that parathyroid extract produces its effect through an increase in the amount of physiologically available diffusible calcium in the serum, though its influence on the phosphorus content must not be forgotten. Another factor which has a definite and demonstrable effect on the diffusible calcium is the protein level of the blood, which forms inert calcium proteinate in direct ratio. We know of no information on this point in connection with papular urticaria.

SUMMARY

A report on a series of sixty patients with lichen urticatus is presented. Thirty-four were given from 10 to 25 units of parathyroid extract subcutaneously at weekly or biweekly intervals. All were given calcium internally, and all but eleven had some topical application. Our results indicate that this is an effective method of treatment, the response being good or excellent in 85 per cent of the patients, as compared with 38 per cent in the control group. The action of parathyroid extract, which seems to be chiefly concerned in the clinical improvement

28. Bakwin, H., and Bakwin, R. M.: Seasonal Variation in the Calcium Content of Infants' Serum, Am. J. Dis. Child. **34**:994 (Dec.) 1927.

29. Oxalic Acid and Calcium Utilization, Current Comment, J. A. M. A. **105**: 440 (Aug. 10) 1935.

30. Holt, L. E., and Fales, H. L.: Calcium Absorption in Children on Diet Low in Fat, Am. J. Dis. Child. **25**:247 (March) 1923.

of the condition of these patients, is the elevation of the level of the calcium content of the blood, which to a large extent is due to an increase in the diffusible or "physiologically available" fraction.

The literature pertaining to the etiology of lichen urticatus is considered in some detail. The theory that the nature of this disease is allergic has been commonly held, and most investigations have been concerned in the attempt to prove or disprove this contention. We believe that the evidence supporting such a view is extremely meager and that further study along the lines of allergy, unless some unique approach is devised, will probably be fruitless.

The favorable influence of parathyroid extract on the course of lichen urticatus may, we believe, be explained either as due to the sedative effect of an increased diffusible fraction of the blood calcium or as a partial or complete correction of some underlying fault in the calcium metabolism. A number of theoretical etiologic possiblities are mentioned which suggest that a further study of calcium metabolism in this disease, especially in relation to the season, temperature, diet and age of the patient, offers the most promising line of investigation.

INTRACUTANEOUS TUBERCULIN TESTS

A COMPARATIVE STUDY OF PURIFIED PROTEIN DERIVATIVE AND OLD TUBERCULIN IN SEVEN HUNDRED AND THIRTY-TWO INFANTS AND CHILDREN

JOHN L. LAW, M.D.
ANN ARBOR, MICH.
WITH THE ASSISTANCE OF CHARLES W. CORY, M.D.

Various surveys of the incidence of sensitization to tuberculin in different countries and in certain communities have had restricted comparative value since the introduction of the tuberculin test more than thirty years ago. Factors vitiating accurate comparison include: (1) variation in clinical material without a statement of its components, i. e., the age group, tuberculous contact or noncontact, urban or rural community with its social status or a particular section of a community and its distinctive features; (2) diversity of technic with the corresponding disparity in sensitivity, i. e., the Pirquet or the Mantoux test; (3) lack of uniformity in the potency of the tuberculin used, i. e., different batches of old tuberculin may vary widely in efficiency since it is not a unit substance and the active principle is seldom the same quantitatively (due to the growth of different strains of the bacillus with the inclusion of nonspecific or protein substances derived from milk or beef peptone medium), and (4) differences in test dilutions of tuberculin used for individual surveys, the resulting percentage of reactors varying with the strength of the tuberculin.

As an indication of the effectiveness of antituberculosis measures, attention is focused on a decreasing mortality rate. A second important index to the effectiveness of the interplay of epidemiological influences is the result of an intracutaneous tuberculin test. This test offers a means of determining the incidence of tuberculin sensitization in any community for different ages at intervals so timed as to make it possible to ascertain if the percentage of positive reactors decreases with improved methods of control and increases with the prevalence of infection. Tuberculin surveys may serve as barometers of changing epidemiological influences exemplified in the lowered incidence of positive reactors at all ages. As an example, twenty-five years ago tuberculin testing among groups of young adults showed approximately 90 per cent of reactors.

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This led to the popular opinion that nearly all young adults have been infected. Recent testing of groups of young adults, entering freshmen in several large universities, showed an average of only 35 per cent of positive reactors.[1] Tuberculin tests or surveys may also indicate the future tuberculosis load in a community by determining the reactors among apparently healthy persons. These considerations and others have led to the recognition of the importance of having a standard potent purified tuberculin material in stated test doses for general use.

As a development of Long's and Seibert's work [2] on the growth of the tubercle bacillus on a synthetic medium, an active protein principle in pure form (purified protein derivative), resulting from the growth of three strains of human tubercle bacilli, has been produced. It meets the requirements of potency, of constancy and probably of specificity.[3] On account of its low molecular weight it is not supposed to sensitize the patient to subsequent test doses.[4] Standard test doses based on comparative tests with various dilutions of purified protein derivative and old tuberculin,[5] using a preparation of old tuberculin of known potency and high activity, have been set and approved by the National Tuber-

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3. Seibert, F. B.: Chemical Composition of Active Principle of Tuberculin: Local Cutaneous Sensitization (Arthus' Phenomenon) Produced in Normal Rabbits and Guinea-Pigs by Protein of Tuberculin, J. Infect. Dis. **51**:383 (Nov.-Dec.) 1932.

4. Seibert, F. B.: The Relationship Between the Sensitizing Properties of Tuberculo-Protein and Its Molecular Weight, Nat. Tuberc. A. Tr. **29**:165, 1933. Barnwell, J. B., and Pollard, H. M.: A Comparison of Old Tuberculin with Tuberculin Protein T. P. T., Am. Rev. Tuberc. **30**:482, 1934.

5. The purified protein derivative used was the product obtained by the method of Dr. Florence B. Seibert from standard synthetic tuberculin medium. The purified protein derivative and the old tuberculin were supplied by courtesy of Parke, Davis & Co.

culosis Association.[6] The first test dose of purified protein derivative, 0.00002 mg., is designed to detect a high percentage of reactors with a minimum of severe reactions. The second test dose, of 0.005 mg., may detect the remaining reactors. The first test dose is supposed to find as many reactors as 0.1 mg. of old tuberculin; the second dose, as many reactors as 1 mg. of old tuberculin.[7]

This report deals with a comparative study of the two standard test doses of purified protein derivative with three dilutions of old tuberculin prepared from a commercial product. The sample of old tuberculin which we used as a standard of comparison was of high activity, as shown by clinical comparison with the old tuberculin used as a standard at the Henry Phipps Institute of the University of Pennsylvania in Philadelphia.[8] In a group of selected patients twenty-five children were tested with the two materials in dilutions of 1 : 1,000 and 1 : 100. The two preparations behaved almost identically as to the size of the cutaneous reactions and do not require tabulation. Two series of tests were then made. In the first series purified protein derivative 1 was compared with 0.01 mg. of old tuberculin and purified protein derivative 2, with 0.1 mg. of old tuberculin. In the second series purified protein derivative 1 was compared with 0.1 mg. of old tuberculin, and purified protein derivative 2, with 1 mg. of old tuberculin.

MATERIAL AND METHOD

The clinical material consisted of 732 children of low economic status who came from households distributed in towns throughout two thirds of the state of Michigan. The majority were hospitalized for the commoner types of medical and surgical diseases. No separation of tuberculous suspects, contacts or those with clinical tuberculosis was made. Suitable physical condition and a temperature under 101 F. were the criteria used in selection of the patients. They were from 1 month to 14 years of age, 38 per cent being from 1 month to 4 years, 48 per cent from 5 to 9 years and 14 per cent from 10 to 14 years. Small series of tests were made on a moving population during 1935 and the early part of 1936.

The solutions of old tuberculin and the purified protein derivative used were freshly prepared every five days and were properly refrigerated when not in use. Tuberculin syringes and fine intracutaneous needles were cleansed between test series with water, weak sodium hydroxide and alcohol and then were sterilized with dry heat. Comparative tests of each subject were made, giving the purified

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7. Hart, P. D'Arcy: The Value of the Tuberculin Test in Man with Special Reference to the Intracutaneous Test, Medical Research Council, Special Report Series, no. 164, London, His Majesty's Stationery Office, 1932.

8. Made available to us through the courtesy of Dr. Joseph D. Aronson.

protein derivative in the left arm and the old tuberculin in the right arm. Each test dose of old tuberculin (contained in 0.1 cc. of solution) was administered intracutaneously. Reactions to the test were noted at the end of twenty-four, forty-eight and seventy-two hours. All patients who showed a negative reaction to both the first dilution of old tuberculin and the first strength of purified protein derivative were retested with the second dilutions of both materials in both series of tests. The reacting area was measured as an average between the longest and the shortest diameter and was recorded in millimeters. Reactions

TABLE 1.—*Summarized Comparison of Old Tuberculin* and Purified Protein Derivtaive† in Four Hundred and Thirty-Two White Infants and Children*

Ages of Children, Years	Number of Children								
	Tuberculin Tested	Showing Positive Reaction to 1:10,000 Dilution of Old Tuberculin (0.01 Mg.)	Showing Positive Reaction to 0.0002 Mg. of Purified Protein Derivative	Showing Positive Reaction to 1:1,000 Dilution of Old Tuberculin (0.1 Mg.)	Showing Positive Reaction to 0.005 Mg. of Purified Protein Derivative	Showing Positive Reactions to Old Tuberculin		Showing Positive Reactions to Purified Protein Derivative	
						Total	Percentage	Total	Percentage
0‡- 4	173	11	15	0	3	11	6.4	18	10.4
5 - 9	199	10	14	2	11	12	6.0	25	12.6
10- 14	60	8	8	0	1	8	13.3	9	15.0
Totals	432	29	37	2	15	31	7.2	52	12.0
Intensity of Reaction, All Ages									
1 plus = 5 — 10 mm.		9	6	1	3	10	32.3	9	17.3
2 plus = 10 — 20 mm.		16	19	0	10	16	51.6	29	55.8
3 plus = 20 mm. or more		4	11	1	2	5	16.1	13	25.0
4 plus = 20 mm. or more with necrosis		0	1	0	0	0	0.0	1	1.9
Totals		29	37	2	15	31	100.0	52	100.0

* First dose, 0.01 mg.; second dose, 0.1 mg.
† First dose, 0.00002 mg.; second dose, 0.005 mg.
‡ The minimum age was 1 month.

were graded according to the method of Aronson: 1 plus, an area of erythema or erythematous infiltration from 5 to 10 mm. in diameter; 2 plus, an area of redness and edema from 10 to 20 mm. in diameter; 3 plus, an area of reaction exceeding 20 mm. in diameter, and 4 plus, an area of reaction exceeding 20 mm., with marked redness, edema and necrosis. In the absence of edema at the site of injection the reaction was considered negative.

RESULTS

Table 1 presents a comparison of the two tuberculins in the first group, consisting of 432 subjects. It is evident that administration of

the first strength of purified protein derivative (0.00002 mg.) found more reactors than did administration of old tuberculin in a dose of 0.01 mg. except in the small group of children from 10 to 14 years of age. Undesirable intensity in reactions occurred so seldom with either tuberculin as to be negligible, one patient with active tuberculosis showing a 4 plus reaction to purified protein derivative. From 70 to 80 per cent of the patients were in the definite but safer 2 and 3 plus reaction group.

TABLE 2.—*Summarized Comparison of Old Tuberculin* and Purified Protein Derivative† in Three Hundred White Infants and Children*

Ages of Children, Years	Number of Children								
	Tuberculin Tested	Showing Positive Reaction to 1:10,000 Dilution of Old Tuberculin (0.1 Mg.)	Showing Positive Reaction to 0.00002 Mg. of Purified Protein Derivative	Showing Positive Reaction to 1:100 Dilution of Old Tuberculin (1 Mg.)	Showing Positive Reaction to 0.005 Mg. of Purified Protein Derivative	Showing Positive Reactions to Old Tuberculin		Showing Positive Reactions to Purified Protein Derivative	
						Total	Percentage	Total	Percentage
0‡- 4	191	5	6	0	1	5	4.9	7	6.9
5 - 9	153	14	16	1	1	15	9.8	17	11.1
10- 14	46	4	4	0	0	4	8.7	4	8.7
Totals	300	23	26	1	2	24	8.0	28	9.3
Intensity of Reaction, All Ages									
1 plus = 5 — 10 mm.		0	0	0	1	0	0.0	1	3.6
2 plus = 10 — 20 mm.		5	11	0	1	5	20.8	12	42.8
3 plus = 20 mm. or more		17	14	1	0	18	75.0	14	50.0
4 plus = 20 mm. or more with necrosis		1	1	0	0	1	4.2	1	3.6
Totals		23	26	1	2	24	100.0	28	100.0

* First dose, 0.1 mg.; second dose, 1 mg.
† First dose, 0.0002 mg.; second dose, 0.005 mg.
‡ The minimum age was 1 month.

In eliciting reactions in those subjects not allergic to the weaker dilutions of tuberculin, the second strength of purified protein derivative (0.005 mg.) was more effective than old tuberculin in a dose of 0.1 mg. Over 700 per cent more positive reactions occurred with purified protein derivative than with old tuberculin. The greatest difference in sensitivity of reaction was found in children from 5 through 10 years of age, among whom were found five times more reactors with purified protein derivative than with old tuberculin. As with the first strength of the materials, the degree of response was largely 2 or 3 plus. There were no 4 plus reactions.

Table 2 records the results of comparative tests of 300 infants and children with the first strength of purified protein derivative and old tuberculin in a dose of 0.1 mg. and the second strength of purified protein derivative and old tuberculin in a dose of 1 mg. It is clear that the number of reactors in all age groups with the first comparative doses is almost the same. With the second strength of the materials there were too few reactors to justify strict comparison. The average intensities of the positive reactions are close for tuberculin in the two forms and the two strengths, with only one undesirable 4+ reaction in each group. More than 90 per cent of the total reactors in the second age group were found with the lesser strengths of purified protein derivative and of old tuberculin.

TABLE 3.—*Total Numbers of Patients Showing Positive Reactions to Various Doses of Old Tuberculin and Purified Protein Derivatives*

Tested with tuberculin	732
Showed positive reactions	80
Showed positive reactions to 0.01 mg. of old tuberculin	29
Showed positive reaction to 0.1 mg. of old tuberculin	25
Showed positive reaction to 1 mg. of old tuberculin	1
Showed positive reactions to old tuberculin	53
Showed positive reaction to 0.00002 mg. of purified protein derivative	63
Showed positive reaction to 0.005 mg. of purified protein derivative	17
Showed positive reactions to purified protein derivative	80
Showed negative reaction to old tuberculin but positive reaction to purified protein derivatives, with roentgenographic evidence of pulmonary tuberculosis	6

Table 3 shows the numbers of patients whose reactions to the various doses of purified protein derivative and of old tuberculin were positive. Twenty-five reacted to purified protein derivatives and not to old tuberculin. Of this number, 6 showed roentgenographic evidence of pulmonary disease (cases 9, 13, 16, 21, 23 and 25 in table 5).

Table 4 summarizes the roentgenographic results of this study. It was found practical to obtain roentgenograms of the chest for only 70 per cent of the reactors.

Table 5 groups the cases according to the types of pulmonary lesions shown in the roentgenograms and details the allergic response to the two tuberculin materials used.

TABLE 4.—*Summary of Roentgenographic Results*

Total number of patients for whom roentgenograms of the chest were made*	55
Total number of patients with no roentgenographic evidence of pulmonary tuberculosis	22
Total number of patients with tuberculous lesions, all types	33
Soft pulmonary infiltration	3
Nonapical strandlike pulmonary infiltration	4
Apical infiltration	7
Pulmonary nodules and uncalcified or partially calcified tracheobronchial lymph nodes	11
Calcified bronchial lymph nodes	8

* It was found practical to take roentgenograms of the chest for only 70 per cent of the positive reactors.

TABLE 5.—*Types of Tuberculous Lesions and Allergic Response of Patients to Old Tuberculin and Purified Protein Derivative*

		Allergic Response of Patients to Old Tuberculin and Purified Protein Derivative							
		Old Tuberculin		Purified Protein Derivative		Old Tuberculin		Purified Protein Derivative	
Roentgenographic Diagnosis	Case No.	First Dose, 0.01 Mg.	Second Dose, 0.1 Mg.	First Dose, 0.00002 Mg.	Second Dose, 0.005 Mg.	First Dose, 0.1 Mg.	Second Dose, 1 Mg.	First Dose, 0.00002 Mg.	Second Dose, 0.005 Mg.
Active lesion									
Miliary tuberculosis	1	0	2+	0	2+	...	...	...	...
Tuberculous pneumonia	2	...	...	...	...	5+	...	3+	...
Apical exudative	3	...	...	...	..	3+	...	3+	...
Nonapical strandlike pulmonary infiltration	4	2+	...	2+	...	...	...	...	...
	5	2+	...	2+	...	...	...	...	...
	6	1+	...	2+	...	...	...	...	...
	7	...	...	...	...	2+	...	3+	...
Apical infiltration	8	...	...	...	...	3+	...	3+	...
	9	...	...	...	...	0	...	2+	...
	10	3+	...	3+	. .	...	...	...	...
	11	1+	...	1+	...	...	...	...	...
	12	1+	...	2+	...	...	...	...	...
	13	0	0	1+	2+	...	...	...	...
	14	1+	...	2+	...	...	...	...	...
Pulmonary nodules and uncalcified or partially calcified tracheobronchial lymph nodes	15	...	...	...	...	3+	...	3+	...
	16	...	...	...	...	0	...	1+	...
	17	2+	...	2+	...	...	...	...	...
	18	2+	...	2+	...	...	...	...	...
	19	2+	...	3+	...	...	...	...	...
	20	2+	...	2+	...	...	...	...	...
	21	0	0	3+	3+	...	...	...	...
	22	0	2+	2+	...	...	...	...	...
	23	0	0	0	3+	...	...	...	...
	24	2+	...	1+	...	...	...	...	...
	25	...	...	...	...	0	...	2+	...
Calcified bronchial lymph nodes	26	2+	...	3+	...	...	...	...	...
	27	1+	...	2+	...	...	...	...	...
	28	2+	...	1+	...	...	...	...	...
	29	0	3+	2+	...	...	...	...	...
	30	2+	...	2+	...	...	...	...	...
	31	...	...	...	...	3+	...	3+	...
	32	...	...	...	...	3+	...	2+	...
	33	2+	...	2+	...	...	...	...	...

COMMENT

From the figures in tables 1 and 2 certain facts emerge which seem to be significant. The giving of the first or second strength of purified protein derivative found all the reactors who were discovered when old tuberculin in any of its three dilutions from 1 : 1,000 to 1 : 100 (0.01 to 1 mg.) was used and also found many more reactors who failed to respond to tests with old tuberculin.

In 432 tests the first strength of purified protein derivative elicited reactions in 37 patients, while 0.01 mg. of old tuberculin found 29 reactors. In 300 tests the use of the first strength of purified protein derivative revealed 26 reactors, and the giving of 0.1 mg. of old tuberculin found 23 reactors. From these figures it seems that the first strength of purified protein derivative corresponds more closely to 0.1 mg. of old tuberculin than to 0.01 mg. in its ability to find reactors.

In comparing the second strength of purified protein derivative with 0.1 mg. and 1 mg. of old tuberculin we found that in 400 tests the use of the second strength of purified protein derivative picked out 15 reactors, while 0.1 mg. of old tuberculin found only 2 reactors. In a series of 275 tests, the giving of the second strength of purified protein derivative found 2 reactors, and 1 mg. of old tuberculin, 1 reactor. This indicates that the second strength of purified protein derivative may be expected to find any reactors found by 1 mg. of old tuberculin.

Since 1 mg. of old tuberculin is the strongest dilution of tuberculin in general use for routine purposes, and since the giving of the second strength of purified protein derivative may be expected to find any reactors revealed by the use of 1 mg. of old tuberculin, nearly all patients sensitized to tuberculin could be found with either the first or the second strength of purified protein derivative.

In 55 tests in which there was a positive reaction to old tuberculin, only 1 patient, or about 2 per cent, had a 4 plus reaction. Of 80 positive reactors to purified protein derivative, only 2, or 2.5 per cent, showed 4 plus reactions. One of these patients had active tuberculosis and when given 0.01 mg. of old tuberculin had the 4 plus reaction. Purified protein derivative, besides being potent and constant, seems to be as safe as old tuberculin and to produce few necrotizing cutaneous reactions.

Table 2 shows that more than 90 per cent of the reactors in this group were found by the first strength of the materials. This is partly explained by the fact that the majority of the positive reactions were in children who had histories of close contact or had tuberculous disease of the bones or the joints. Also it indicates the effectiveness of the first strength of purified protein derivative in finding reactors who have some form of tuberculous lesion.

Table 5 shows that 6 patients with roentgenographic evidence of pulmonary tuberculosis reacted to purified protein derivative and not to old tuberculin. None of the 6 was tested with the strongest dilution of old tuberculin, namely, 1 mg. It is, therefore, possible that had they been given 1 mg. of old tuberculin they would have shown a positive reaction. However, 5 patients (cases 9, 13, 16, 21 and 25 in table 5) reacted negatively to 0.1 mg. of old tuberculin and positively to the first strength of purified protein derivative. Only 1 patient (case 23 in table 5) showed a positive reaction to purified protein derivative and a negative reaction to old tuberculin when the second strength of purified protein derivative was used in comparison with 0.1 mg. of old tuberculin. This seems significant, for, as shown earlier, 0.1 mg. of old tuberculin and the first strength of purified protein derivative may be expected to pick out about the same number of reactors.

The facility with which the purified protein derivative in tablet form can be handled and diluted for a quantitative intracutaneous test is admirable. Adoption by the National Tuberculosis Association of a purified protein tuberculin derivative in standard test doses and its universal use will help to clarify the position of the medical profession in regard to the changing incidence of sensitization to tuberculin as related to epidemiological influences in various communities and in certain age groups.

The newer conception that an allergic response to tuberculin in a child is a warning of increased susceptibility to tuberculosis may prove to be important.[9] Emphasis may be placed on the value of uncontaminated normal tissue in the prophylaxis of phthsis. The intracutaneous tuberculin test with an error of 2 per cent in the negative diagnosis of tuberculous infection may attain wider general use as the result of the availability to the practicing physician of a potent, stable and easily diluted product. Great good may proceed from detecting the primary infection at its inception by use of the tuberculin test. Rest and adequate hygiene may then circumvent the sudden development of an occasional grave manifestation of a primary infection, such as miliary tuberculosis or tuberculous meningitis, as pointed out by Wallgren;[10] sufficient rest and competent supervision, including the periodic taking of roentgenograms during childhood, may also hinder or prevent altogether the development of phthisis in adulthood.

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9. Stewart, C. A.: Pathogenesis of Tuberculosis in Man: Certain Governing Principles and Causal Relationships Existing Between Primary and Reinfection Types of Disease, Am. J. Dis. Child. **50**:853 (Oct.) 1935.

10. Wallgren, A.: Some Aspects of Tuberculous Meningitis and Possibility of Its Prevention, J. Pediat. **5**:291, 1934.

SUMMARY

The behavior of purified protein derivative in its two standard test doses in comparison with three dilutions of potent old tuberculin in about 3,000 tests show that the purified protein derivative is uniform in its reaction, potent and reliable. The first strength of purified protein derivative (0.00002 mg.) found more reactors than did old tuberculin in a dilution of 1:10,000 (0.01 mg.), or about the same number of reactors as did old tuberculin in a dilution of 1:1,000 (0.1 mg.).

The use of the second strength of purified protein derivative (0.005 mg.) found over seven times more reactors than did the administration of old tuberculin in a dilution of 1:1,000 (0.1 mg.), whereas the giving of the second strength of purified protein derivative found twice the number of reactors revealed by old tuberculin used in a dilution of 1:100 (1 mg.).

Purified protein derivative is well adapted for accurate quantitative tests, which seldom give necrotizing skin reactions.

It is admirably suited for general use and for epidemiological studies related to the control of tuberculosis.

EXTENSIVE XANTHOMA TUBEROSUM IN CHILDHOOD DUE TO INFECTIOUS CIRRHOSIS OF THE LIVER

DEVELOPMENT OF XANTHOMATOUS CHANGES IN LAPAROTOMY AND OTHER SCARS

FRED D. WEIDMAN, M.D.
AND
JOSEPH STOKES JR., M.D.
PHILADELPHIA

The rôle of the liver, particularly when it is characterized by hypertrophic cirrhosis, in the development of cutaneous xanthoma has been so thoroughly established that it needs little discussion in this paper. It is the study of other, associated features which should add to the knowledge of the nature of xanthomatous changes. As to the precise classification of the condition in our case of xanthoma, one's first thoughts turn to Christian-Schüller's disease or related xanthomatous states. However, it will be indicated in succeeding pages that such essential symptoms of Christian-Schüller's syndrome as lesions of the bones and exophthalmos were absent. Likewise, the comparatively common juvenile xanthoma, which often occasions so much diagnostic difficulty for the dermatologist in connection with urticaria pigmentosa, was promptly eliminated from consideration by the profound general systemic accompaniments. It seemed wiser, therefore, to refer to and classify the condition as xanthoma tuberosum as it occurs in adults, some expressions of which are notoriously associated with hypertrophic biliary cirrhosis.

On such a basis, the incidents of value in this child's case which made it distinctive were as follows: First, histologic examination of the liver at a comparatively early date, early even in the life of a child, was made possible through the performance of an exploratory laparotomy. Secondly, it was demonstrated that the blood cholesterol content could rise to a great height, i. e., 1,199 mg. per hundred cubic centimeters. Thirdly, the case afforded an additional instance of the development of xanthoma in young growing fibrous tissue, e. g., in the laparotomy scar and in the gums after extraction of the teeth. Finally, the symptom complex illustrated that the range of symptoms of xanthoma is not

From the Laboratory of Dermatological Research and the Department of Pediatrics, University of Pennsylvania School of Medicine.

sharply defined. For example, an attempt has been made by some authors to classify in a single group conditions characterized by lipoidal changes such as those in Christian-Schüller's disease, in Gaucher's disease and in the Niemann-Pick syndrome, as well as in what Helene Herzenberg designated as the skeletal form of Niemann-Pick's disease.[1] In our case, the high cholesterol content of the blood, the xanthomatous changes, the disease of the liver and the diabetes insipidus definitely related the condition to one or the other of the foregoing groups. We will discuss in subsequent paragraphs the interrelationships of these different syndromes; at the same time we will show in detail why we believe that the condition in our case should be classified otherwise than as Christian-Schüller's disease.

REPORT OF A CASE

History.—Bernice B., a girl born Aug. 25, 1922, applied for medical relief on Nov. 2, 1926, with the chief complaint of enlargement of the abdomen. An aunt had diabetes; two sisters (8 and 9 years old) were living and well. The mother had been slightly jaundiced during pregnancy and suffered from some dizziness. The child was artificially fed from birth. Milk diluted with barley water and Mellin's Food did not agree well with her during the first seven months, and she was shifted to malted milk, which between the ages of 7 months and 2 years was her only food except orange juice, which was added to the diet when she was 1 year old. She held up her head at the age of 4 months and sat up at 7 months; the first teeth appeared at 8 months, and she walked alone at 17 months.

She was an inactive child. A tonsillectomy was performed when she was 3 years old. She had whooping cough at the age of 18 months and measles at 3 years, with uneventful recoveries. Recurrent soreness of the eyes and more severe soreness of the gums had been present for the previous one and a half years.

About twenty months before admission (when the child was about 2 years old) the mother noticed a marked increase in her thirst, both for milk and for water. Fourteen months before admission her thirst had begun to result in the drinking of from 3 to 4 quarts (from 2.8 to 3.8 liters) of water at night, as well as many quarts during the day. On account of this thirst and the voiding of large amounts of pale urine she was taken to a hospital, where she remained for five weeks' study. She weighed 26½ pounds (12 Kg.) on admission and 22½ pounds (10.2 Kg.) on discharge, and a final note was made at the hospital that the diagnosis was diabetes insipidus and that her condition was unimproved.

Six months later she was admitted to a second hospital, where she remained for seven months. From this hospital she was discharged to the University of Pennsylvania Hospital with a note that her urinary output had decreased considerably, owing chiefly to the withholding of fluids; that her polydipsia had improved after effective treatment of her gums and buccal mucous membranes, which on culture had revealed many Vincent organisms, and that her liver had increased somewhat in size. Enlargement of her liver had been noted at the time of her original hospitalization.

1. Herzenberg, H.: The Skeletal Form of Niemann-Pick's Disease, Virchows Arch. f. path. Anat. **269**:614, 1928.

Examination.—The patient was admitted to the University of Pennsylvania Hospital Nov. 2, 1926, to the service of Dr. J. C. Gittings, who permitted us to report the case. She was a small child, 33 inches (83.8 cm.) in height, with signs of emaciation but a protruding abdomen. Her skin was sallow and dry, with moderate desquamation over the lower extremities. The lips were parched and fissured. She had no fever. The hair was decidedly scanty, the frontal bones were prominent and there was slight seborrheic dermatitis. The circumference of the head was 20 inches (50.8 cm.), that of the chest 20 inches (50.8 cm.) at the nipple line and that of the abdomen 21 inches (53.3 cm.).

The conjunctivae were slightly red and the scleras distinctly icteric. The tongue had a gray furry coating, probably the result of the inflammation about the teeth and gums, and several of the teeth were carious. There was a postnasal discharge, and the tonsils were fairly large and moderately reddened.

The submaxillary and anterior cervical glands were slightly enlarged.

Except for slight beading of the costochondral junction and evidence of emaciation, the chest was normal.

In the protruding, thin-walled abdomen the spleen was readily palpable. The liver, with a sharp, firm edge, could be felt filling the entire upper right quadrant and reaching 3 inches (7.6 cm.) below the costal margin.

Laboratory Report at Admission.—The Wassermann reaction of the blood was negative. A tuberculin test, with 0.01 mg. injected intradermally, did not cause any reaction. Smears from the gums showed many Vincent organisms. A differential count showed red blood cells 4,720,000, white blood cells 22,300, hemoglobin content 86 per cent, polymorphonuclears 58 per cent, lymphocytes 35 per cent transitional forms 3 per cent and eosinophils 4 per cent. The direct van den Bergh reaction was negative; 1 unit was found by the indirect test. The specific gravity of the urine was 1.005. There was a faint trace of albumin, but no sugar. Urobilin, bilirubin, casts and red blood cells were absent. There were a few white blood cells, with clumping.

The response to the sugar tolerance test was as follows:

	Blood Sugar Mg. per 100 Cc.	Urinary Sugar
Fasting	110	0
Half hour after 18 Gm. of dextrose	125	0
One hour after 18 Gm. of dextrose	143	Trace
Two hours after 18 Gm. of dextrose	100	0

Much occult blood was found in the stools.

Soon after the child's admission four deciduous teeth and one premolar tooth were extracted, and the inflammation about the gums began to subside, although Vincent organisms continued to be abundant and the inflammation was still marked. On this account 0.08 Gm. of neoarsphenamine was injected intravenously on Dec. 3, 1926. A second injection of the same amount was made on the tenth of that month. The abdomen at this time was 22 inches (55.8 cm.) in circumference; the gain in weight was 1 pound (0.5 Kg.); the quantity of urine passed was large (from 2,500 to 3,000 cc.), and the specific gravity of the urine was low.

Roentgenograms of the chest, the jaws and the sella turcica revealed nothing pertinent.

A permanent molar on the left side of the upper jaw became loose soon after the child's admission, and in two months the left upper and lower first molar and

right upper first molar were extracted. Thereafter, the condition in the mouth improved rapidly. Several urine concentration tests at this time revealed that the specific gravity never rose above 1.015, while a phenolsulfonphthalein test indicated 50 per cent excretion in two hours. The blood pressure remained at about 96 systolic and 72 diastolic.

With an increase in the circumference of the abdomen to 25 inches (63.5 cm.) the icterus increased, urobilin and bilirubin appeared in the urine and the van den Bergh test showed an immediate direct reaction and an indirect reaction of 2.9 units. A fragility test showed that hemolysis began with a 0.45 per cent solution of sodium chloride and was complete with a 0.325 per cent solution.

Exploratory Laparotomy.—On account of the increasing jaundice, the enlargement of the liver and the spleen and the complete failure of the child to gain weight, an exploratory laparotomy was performed by Dr. Brill, of Dr. George Müller's service, April 19, 1927. A large and nodular but fairly soft liver was found, with evidence of definite cirrhosis; a small piece was removed for microscopic examination. The spleen was slightly enlarged. Ascites was not recorded.

Histologic Picture of the Liver.—The section submitted measured 1 cm. in diameter. The capsule appeared normal. The perilobular fibrous tissue was of normal thickness in places but for the most part was markedly broadened. While the thickening was largely referable to an increase in the fibrous tissue, hyperplasia of the bile ducts played a large part. The predominant cells were of the spindle-shaped type; lymphoids and polymorphonuclears took second place. The nuclei of the spindle cells were singularly deformed, and the cells approached the shape of endothelioid cells. However, their nuclei were pyknotic and consisted almost solidly of chromatin, so that they were not pallid, like endothelioid cells.

The lobules of the liver varied markedly in size; some were but 0.5 mm. in diameter, while the limits of others could not be defined because they merged with neighboring cells. However, both the smaller and the larger lobules consisted of hugely swollen parenchymal cells the cytoplasm of which was rarefied and uniformly studded with coarse pink granules. The swelling was so extreme that the outlines of hepatic cords could be made out only in certain places; the blood sinuses were largely obliterated, with the result that extensive areas exhibited only a uniform sheet of closely packed, more or less polygonal liver cells. The tissue thus resembled more the pars fascicularis of the adrenal or the corpus luteum than liver. At the periphery of the lobules the nuclei contained increased quantities of chromatin, the amount of cytoplasm was smaller and the cells approached closely in character the epithelium of the bile ducts. Indeed, at times such formations could be traced into connections with the hyperplastic ducts in the capsule of Glisson. The nuclei of the large, clear parenchymal cells were circular and sharply defined and stained distinctly; in short, they appeared normal.

In the relatively few positions where blood sinusoids could be identified, the cells lining their walls were condensed to the extent that, while they did not comprise a definite lining, a cuticle nevertheless separated them from the parenchyma. The sinuses contained, for the most part, ghost corpuscles; but in addition there were red blood cells sufficiently well preserved to indicate that the ghost elements were not artefacts. The normal red cells stained intensely pink and were sharply outlined. Kupffer cells also appeared in the sinuses, so swollen at times as to be larger than the parenchymal cells, swollen as the latter were. The nuclei were generally degenerate and the cytoplasm rarefied and reticular. The latter was often crowded with bile pigment; indeed, the cytoplasm of the smaller Kupffer cells appeared to be occupied solidly by it. Bile pigment also appeared in the

dilated bile canaliculi in the axis of the hepatic cords and in smaller quantities in the parenchymal cells themselves.

Blood pigment was utterly absent; singularly, bile pigment did not appear in either the fibrous tissue or the ducts of Glisson's capsule.

Interpretation of the Histologic Picture.—There was clearcut hypertrophic biliary cirrhosis together with an enormous expansion of the parenchymal cells by material which was doubtless lipoid. While polymorphonuclear cells were discoverable in the neighborhood of the hyperplastic bile ducts, their number was

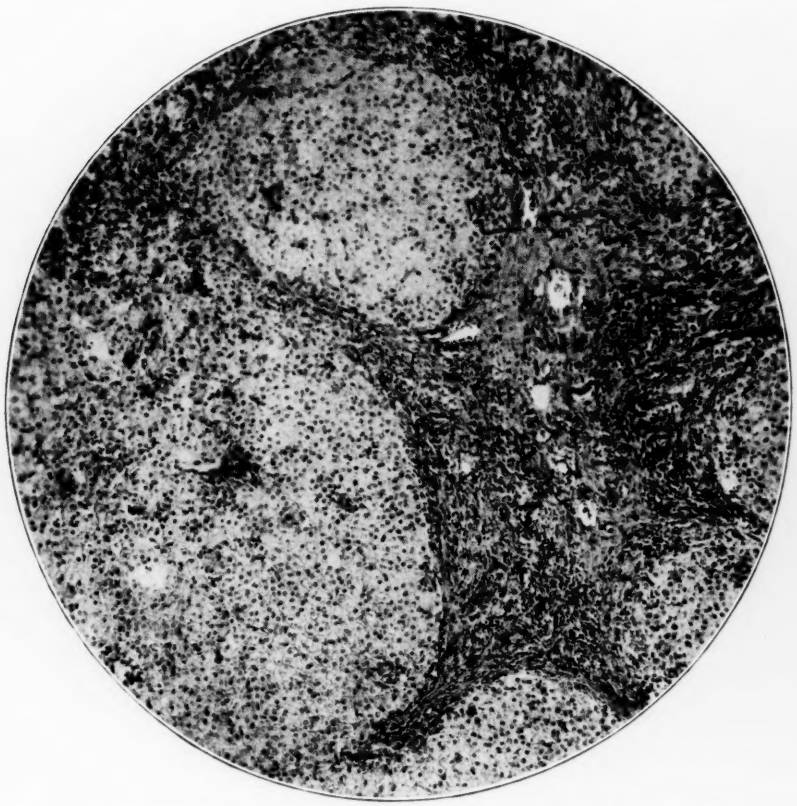

Fig. 1.—Section of cirrhotic liver, illustrating the high degree of change (variation in the size of the lobules, thickening and cellular infiltration of Glisson's capsule).

not great. The absence of bile in connection with the ducts spoke against an obstructive factor in the biliary system; more likely, the extreme swelling of the parenchymal cells was the factor retarding the flow of bile. It is proper to speculate whether the presence of ghost cells (connoting the destruction of blood) was related to the excess of lipoidal substance in the parenchymal cells; we doubt that the anesthesia incident to surgical intervention was a complicating and contributing factor. We feel satisfied, however, that at least at the time of the operation there was a state of unequivocal damage to the red blood cells.

Course.—On examination on May 6, 1927, the jaundice was more marked, and although the urine at this time was free from urobilin or bilirubin, the van den Bergh test showed a definite increase in the immediate direct reaction and 4 units by the indirect reaction. The abdomen had increased in size. The polyuria and the polydipsia were not as marked.

On June 9 several lower teeth which had become loose as a result of pyorrhea were extracted.

On July 5 the van den Bergh test showed an immediate direct reaction and an indirect reaction of 8 units.

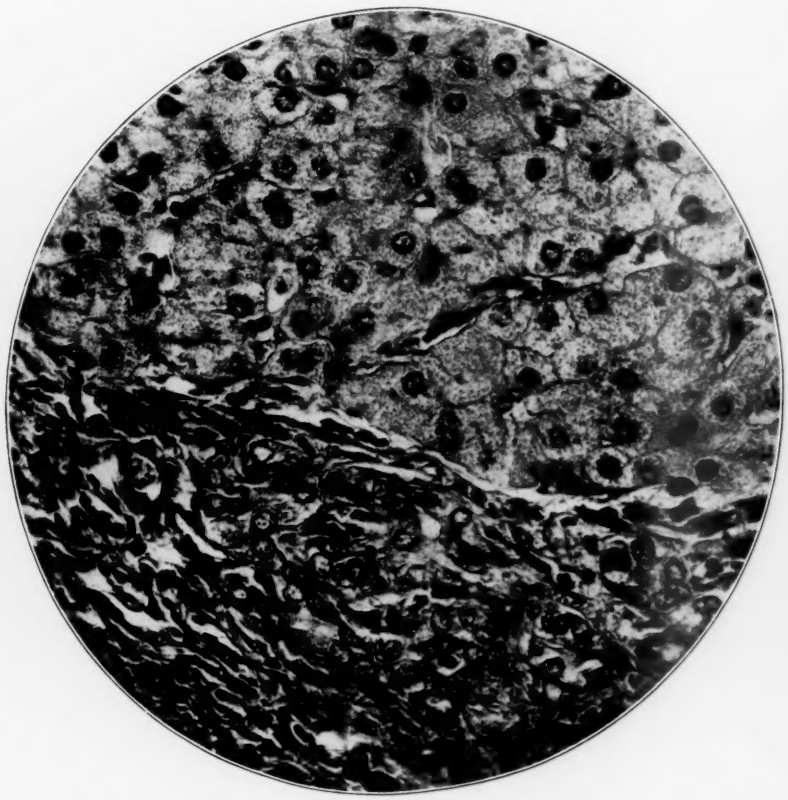

Fig. 2.—Section showing extreme narrowing and obliteration of blood sinusoids in the liver by hugely swollen (xanthomatous) parenchymal cells. The prominent spheroidal nuclei in the (hyperplastic) capsule of Glisson, below, are of young hyperplastic bile ducts.

On July 16 four more teeth were extracted.

On August 8 multiple minute xanthomas began to appear over the entire body. A few, as large as 5 mm. in diameter, had been noticed immediately after the operation. In addition, some appeared on the upper eyelids, the gums and the operative scar; none appeared at the site of an old antismallpox vaccination. The original position of practically every tooth was marked by one or two yellow

nodules from 1 to 4 mm. in diameter. The laparotomy scar measured about 10 cm. in length and 1.5 cm. in width and projected well above the cutaneous surface. It was diffusely and frankly yellow. Special nodules were not present in the major scar, but nodules at the stitch holes gave a striking appearance to the lesion.

On August 16 four more teeth were extracted, and on the next day the blood cholesterol content was 1,199 mg. per hundred cubic centimeters. On August 23 it was 1,067 mg. Several other determinations had been made before these highest values were found, and the earlier examinations showed a slowly increasing retention of the cholesterol in the blood.

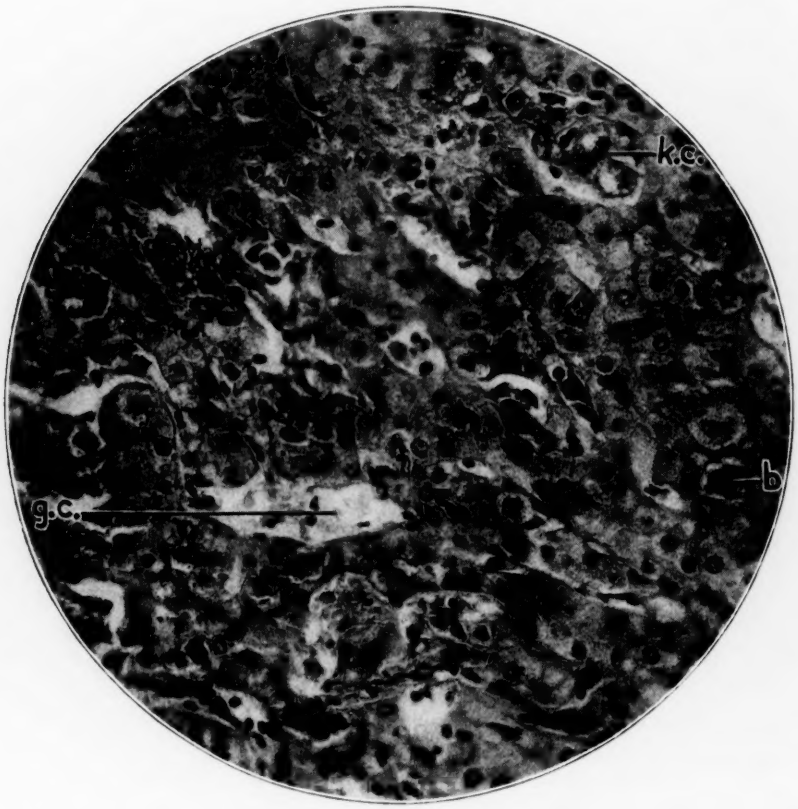

Fig. 3.—Section of a comparatively nonxanthomatous part of the liver. The magnification is the same as that in figures 1 and 2. *G.c.* indicates ghost corpuscles in a sinusoid; *k.c.*, a Kupffer cell (foamy), and *b.*, plugging of a bile canaliculus by bile.

The icterus index was 80. The liver function test (with bromsulphalein) showed that the blood serum contained from 15 to 20 per cent of the dye after half an hour.

On September 2 the remaining teeth were extracted. Slight polyuria was still present. The bladder at one urination discharged 690 cc. of urine. The urea nitrogen content of the blood was 17 mg. per hundred cubic centimeters.

On September 27 the van den Bergh test showed an indirect reaction of 10 units. The icterus index was 125 units.

One month later a liver function test with epinephrine was performed. There was no rise in the blood sugar content after 0.5 cc. of a solution of epinephrine hydrochloride (1 : 1,000) was injected subcutaneously (determinations of the blood sugar were made every half-hour for two hours). Moderate anemia of a secondary type had developed.

Final Notes.—After discharge to her home, April 17, 1928, the patient began almost immediately to suffer from epistaxis. In August she had five hemorrhages in one week, losing over a "bucket of blood" with each one. From this time until

Fig. 4.—Photomicrograph of a Kupffer cell in a hepatic sinusoid. It is hugely swollen and contains bile pigment and lipoid vacuoles.

December she had fifteen more hemorrhages. Polydipsia became more and more pronounced. Before her death she was drinking about 12 quarts (113 liters) of water daily and 6 quarts (56 liters) nightly. During this time she was never bedfast; she appeared bright and lively until her death. She died while taking her afternoon nap at home on June 10, 1929. Necropsy was not performed.

CLINICAL SUMMARY

A 4 year old child exhibited a group of symptoms which in certain respects were suggestive of Christian-Schüller's syndrome: diabetes insipidus, jaundice, loosening of the teeth, hypercholesteremia and hepatomegaly. Of important symptoms, exophthalmos and disease of

the bones (at least of the skull) were lacking; since the latter is a sine qua non for Christian-Schüller's syndrome, we feel that the condition in our case probably cannot be admitted to that category.

In respect to the bones, only one roentgen examination was made of the skull and no examination was made of the pelvis or the long bones, which is unfortunate in view of the fact that this patient gave evidence of two symptoms common in Christian-Schüller's syndrome, namely, diabetes insipidus and loosening of the teeth. However, the diabetes insipidus was well established when the roentgenogram of the skull was taken, and if the typical deformities of the membranous bones had been present they certainly would have been evident in these films. There was no evidence at any time of exophthalmos, which also militates to some extent against the diagnosis of Christian-Schüller's disease. We realize, however, that exophthalmos is not necessary for the diagnosis if the roentgen findings are typical.

It is altogether proper to speculate on the rôle of the arsenicals intravenously administered in accelerating the cirrhosis and jaundice, since there was little evidence from the van den Bergh test and only a slight icteric coloring of the scleras to show that the liver had been damaged previously. However, the liver was already definitely enlarged when the intravenous injections were made, even though the van den Bergh test showed a marked increase in the indirect reaction soon afterward.

The oral infection could account for the loosening of the teeth. At the time of extraction the fatty pads at the roots of the teeth so frequently noted in Christian-Schüller's disease were not present.

Treatment was based mainly on the supposition that the infection in the mouth and the consequent absorption of the bacteria and the toxins which were continuously draining into the intestinal tract might account for the cirrhotic reaction of the liver. To rid the mouth of the foul infection was the object of the radical extraction procedures and the medical treatment employed.

DIFFERENTIAL DIAGNOSIS

It is unfortunate that a necropsy was not performed on this patient, since morbid anatomic changes in the viscera are so definitely diagnostic in cases of the xanthomatous conditions mentioned previously. However, a sufficient accumulation of clinical information remained to enable us to compare the processes in our patient with those in patients with related lipoidal dyscrasias. The absence of changes in the skull made the diagnosis of Christian-Schüller's disease most improbable. Niemann-Pick's disease could be eliminated in view of the absence of neurologic signs and splenomegaly. Also, the histologic examination

of sections of the liver revealed none of the foam cells which are characteristic of Niemann-Pick's disease and occur in large numbers throughout the liver when that disease is present.

Gaucher's disease also affects the liver, and splenomegaly is one of its cardinal signs, but in this case sections of the liver showed none of the giant cells filled with kerasin which are typical of the disease. Also, Gaucher's disease rarely occurs in a fatal form at the age of our patient, and when it is of a fatal type the spleen holds the foreground of the disease picture.

Certainly icterohemolytic anemia of the familial type could not be seriously considered, for two important reasons. First, the fragility of the red blood cells in a hypotonic saline solution was normal, and, second, there was no splenomegaly. In addition, it should be mentioned that the van den Bergh test showed an immediate direct reaction, which is rarely present in cases of icterohemolytic anemia.

In the later stages of Banti's disease (splenic anemia) the spleen is usually fibrotic, and there may be only slight enlargement, with accompanying signs of jaundice and of an enlarged cirrhotic liver, a state which was in a large part present in our case. The hemorrhages were also consistent with the findings in our case. Banti's disease could not be ruled out entirely in our case without an autopsy, and yet the age of the patient was well below that in the usual case. In splenic anemia, hypercholesteremia and xanthoma are rare, the cirrhosis of the liver is more biliary than atrophic (Laënnec's cirrhosis) and an early enlargement of the spleen is a necessary part of the picture.

It appears, then, that the condition in our case cannot be assigned outright to any of the syndromes described. If one divested it of its xanthomatous features, it would have approached Banti's disease more closely than any of the other syndromes or, stated in another way, it is understandable (taking into account the variations common to all syndromes) that Banti's disease with superadded hypercholesteremia and xanthomatosis could approach the complex seen in our patient.

PATHOLOGY

In the light of what is already so thoroughly established for the pathogenesis of adult xanthoma tuberosum, it is proper to begin with the liver in tracing the pathogenesis in this child. The histologic examination of sections of the liver left no doubt as to the definiteness of the biliary cirrhosis, and both the pediatric and the surgical examination added the fact that the liver was hypertrophic. Even in the absence of necropsy it appears to be final, then, that hypertrophic biliary cirrhosis (probably infectious) was fundamental to the entire complex. The hypercholesteremia is therefore readily understandable, being a con-

sistent development in jaundice in adults and a frequent accompaniment of this form of cirrhosis.

The next step in the pathogenesis is the development of cutaneous depots of cholesterol (xanthoma). It is out of place to comment here on the intricacies of this subject; suffice it to say that in our case events probably followed the course conventionally assigned to xanthoma tuberosum. In brief, in the presence of hypercholesteremia, excess lipids are deposited in cells which are predisposed to receive them.[2]

However, special attention must be directed to the rôle of scar tissue in determining the localization of xanthomas because our patient certainly had scars in the gums, as well as in a laparotomy wound. A full discussion of xanthomatous changes in scars, including a catalog of pertinent cases, appeared in Weidman and Boston's report.[3] Xanthomas in the scars subsequent to zoster, syphilis, punctures with hypodermic needles, mosquito bites and herniotomy wounds, as well as in more diffuse formations of granulation tissue such as those succeeding erysipelas, have already been described.

For the pediatric field, only the case of Artom[4] merits abstracting here. The child had exhibited xanthomatous change in a herniotomy scar; in addition, a number of xanthomas had appeared for some distance outward in the neighboring skin. Intercurrent generalized exfoliative dermatitis developed in the child; when it regressed, not only the residual nodules of xanthoma but plaques of *diffuse* xanthomatous change remained.

It thus appears that young, rapidly dividing fibrous tissue cells are in a particularly favorable (basal metabolic?) state to accept, or at any rate to exhibit, the fatty accumulations which result in xanthomatous phenomena. Such cells are characteristic of all lesions of the types cited. The premise is correct whether the fibrous tissue is distributed focally, as in scars, or diffusely, as in erysipelas. It is therefore easy to understand why the teeth of young, growing children should determine the localization of xanthomatous changes. The gums are in a position of

2. A large amount of literature has developed on the subject of the "predisposition" of cells to xanthomatous infiltration (Pinkus, F., and Pick, L.: Xanthoma and Foam Cell Tumors, with Report of a Case of Generalized Xanthoma Tuberosum, Dermat. Ztschr. **15**:706, 1908. Schmidt, E.: Beiträge zur Xanthomfrage, Arch. f. Dermat. u. Syph. **140**:408. 1922. Weidman, F. D.: Xanthosarcoma of the Cheek Succeeding Xanthosarcoma of the Forearm, Arch. Surg. **34**:792 (May) 1937.

3. Weidman, F. D., and Boston, L. N.: Generalized Xanthoma Tuberosum with Xanthomatous Changes in Fresh Scars of an Intercurrent Zoster: Andenocarcinoma of the Ampulla of Vater at Necropsy, Arch. Int. Med. **59**:793 (May) 1937.

4. Artom, M.: Papular Xanthoma, Gior. ital. di dermat. e sif. **68**:1060, 1927.

pressure and stress (expansion of teeth, eruption of teeth and replacement of deciduous teeth), which occasion the presence of cells in a proliferative state. The physiologic scar at the umbilicus and the anti-smallpox vaccination scar are, conversely, likely to be composed of fibrous tissue cells which are *quiescent* and therefore not amenable to the xanthomatous processes. We feel, however, that if subjects with hypercholesteremia were vaccinated for smallpox, xanthomas would probably remain in the scar, just as they did in Ochs'[5] case. Vaccination would be well worth trying as a harmless experiment in future cases of xanthoma, particularly if associated hypercholesteremia is present.

The factor of scars brings up the rôle of preexistent lesions in determining the localization of xanthomas even though the sequelae are not visible as scars. In the preceding comments we emphasized not only the scar but the particular metabolic state of the cells comprising it. Conceivably, a local group of cells which has passed through the violent changes incident to inflammatory reactions could be modified in the direction of lipid dyscrasia, just as other local groups of cells can become immunologically or otherwise altered. For example, epidermal cells in old syphilitic scars become pigmented in a way in which they normally would not. There are local immunities against experimental reinoculations with fungi at the sites of preceding lesions that do not obtain elsewhere on the skin. In the field of allergy, reingestion of phenolphthalein provokes dermatosis at the precise sites of previous eruptions caused by phenolphthalein—the erythema perstans of the dermatologist.

These thoughts are provoked by consideration of Lehzen and Knauss' two patients.[6] One of the sisters had "festers" all over the body at the age of 3 years. They disappeared; the xanthomatous lesions appeared at the age of 4. Xanthoma developed in the other sister at the termination of a vesicular eruption. Certainly in the latter child the scars were fresh.

Cases such as these suggest a much needed explanation for the localization of lesions (more or less symmetrical) in juvenile xanthoma, in which the distribution differs from that in adult xanthoma tuberosum. Indeed, with the yellow (lipoidal) factor satisfactorily explained, one should consider particularly the *distribution* and the anamnesis of the lesions and determine whether they can be reconciled with those of already recognized forms of dermatosis. Thus far we have not been

5. Ochs, B.: Xanthoma Tuberosum, Arch. Dermat. & Syph. **22**:922 (Nov.) 1930.

6. Lehzen, M., and Knauss, B.: Ueber Xanthoma multiplex planum, tuberosum, Mollusciforme, Virchows Arch. f. path. Anat. **116**:85, 1889.

successful for juvenile xanthoma, although the recognition of a nevic basis is promising.[7]

Xanthomatous scars thus demonstrate that the xanthomatous features are but superadded on lesions of a type already well known to the pathologist, and were the scars not too obvious the xanthoma could be so highly developed as to mask completely the nature of the original underlying process. It is a question how much further the idea can be carried. If it is conceded that scars and nevi are liable to a disguise of the kind described, it remains for the future to determine whether other lesions, or even sets of lesions, like multiple myeloma, can participate in a similar order of change. In such cases, established symptom complexes like multiple myeloma could pass undiagnosed because xanthomatosis was superadded and masking them. This fact calls for reexamination and analysis in a new light of lipoidal dyscrasia like that in Christian-Schüller's disease [8] and in related xanthomatous states.

Pathologic Classification.—Because the patient was a child it was eminently desirable to compare her condition with Christian-Schüller's disease, but, as explained in the section on differential diagnosis, the condition could not be referred to any of the xanthomatous diseases thus far established except xanthoma tuberosum of adults. The question arose next as to the scope and the limitations of the Christian-Schüller syndrome, since, if it were made broad enough, it could extend to and include our case.

It is not within the province of this paper to review the premises of Christian-Schüller's disease in detail and to attempt to clarify such an involved syndrome, of which the etiology is not established. We have analyzed to a certain extent many of the cases which were reviewed by Rowland,[9] and we feel that several of them (those of Weidman and Freeman [8] and Herzenberg [1]) when grouped with the one we now report indicate that the Christian-Schüller classification is only temporary and is perhaps artificial. That is, it is not homogeneous either semeiologically or biologically. Temporarily, we feel, the Christian-Schüller concept merits acceptance as a convenient designation (for which Christian deserves credit), but with the reservation that, like Hodgkin's disease, the syndrome may not be an etiologic entity. The views expressed in the section on the pathologic picture which indicate the

7. MacDonagh, J. E. R.: Naevo-Xantho-Endothelioma, Brit. J. Dermat. **24**: 85, 1912. Weidman, F. D., and Schaffer, H. W.: Xanthoma of the Skin and Larynx, Associated with Carcinoma of the Stomach and a Regressive Xanthoma of the Pons, Arch. Dermat. & Syph. **35**:767 (May) 1937.

8. Weidman, F. D., and Freeman, W.: Xanthoma Tuberosum, Arch. Dermat. & Syph. **9**:149 (Feb.) 1924.

9. Rowland, R. S.: Christian's Syndrome and Lipoid Cell Hyperplasia of the Reticulo-Endothelial System, Ann. Int. Med. **2**:1277 (June) 1929.

possibility of classifying xanthomatous syndromes according to some underlying nonxanthomatous disease process which might be disguised by the superimposed or concomitant lipoidal changes have a bearing here. If this classification could be achieved, it would reduce the number of cases classifiable under Christian-Schüller's disease and leave under that heading only cases in which the condition can be classified as a disturbance affecting the so-called reticulo-endothelial system. To what extent this classification is possible remains to be determined.

Comparison of Syndromes Involving Xanthoma

	Banti's Disease*	Weidman and Stokes	Multiple Myeloma*	Herzenberg†	Weidman and Freeman	Christian-Schüller's Disease
Familial	?	—	?	+	—	—
Mortality	++++ (Early)	++++ (Early)	++++	++++	++++ (Early)	++++ (Early)
Hypercholesteremia	—	++++ (1,199 mg.)	?	Not tested	(397 mg.)	++—
Skin	—	+++	—	++	++++	— (Scabies-like)
Hepatic disease	++++	+++	—	+	++++	++
Splenomegaly	++++	+	—	+	+++	+
Bones	—	—	++++	+++	++++	++++
Type of bone	—	—	Flat	Long and flat	Flat	Flat
Adenopathy	— Hemo-lymphatic	—	—	++	+ Hemo-lymphatic	—
Exophthalmos	—	—	++	—	++++	++—
Jaundice	++	++++	—	—	++++	Rare
Diabetes insipidus	Glycosuria	++++	++ or —	+++	++++	++++
Ascites	+++	—	—	—	+++	

* Not xanthomatous, but included in connection with other symptoms common to the group.

† Skeletal form of Niemann-Pick's disease; subsequently claimed to be tuberculosis by O. Lubarsch. (Remarks on the Work of H. Herzenberg: The Skeletal Form of Niemann-Pick's Disease, Virchows Arch. f. path. Anat. **269**: 823, 1928.)

In any event, we believe that, in line with the thoughts expressed in the section entitled "Pathology," the original reports of the cases listed in any complete catalog of case histories of Christian-Schüller's disease which may be available merit reexamination and analysis. Such a study might lead to the detection of definite disease entities apart from abnormalities which were fundamentally reticulo-endothelial. In the interest of rational classification, future cases deserve study in the direction more of underlying tuberculosis, multiple myeloma, Hodgkin's disease, Banti's disease, granuloma fungoides, aleukemic leukemia and chlorosis than of the altogether obvious xanthomatous phase.

The table illustrates the similarity between Christian-Schüller's syndrome and certain other diseases on which we have already commented.

SUMMARY AND CONCLUSIONS

A fatal case of jaundice and cutaneous xanthomatosis due to hypertrophic biliary cirrhosis in a child is described. The syndrome was differentiated from Christian-Schüller's disease and finally referred to a complex, xanthoma tuberosum, which occurs in adults in connection with cirrhosis of the liver. Items which attracted special attention were the exceedingly high value for blood cholesterol (1,199 mg. per hundred cubic centimeters), the development of xanthomatous changes in the scars of a laparotomy wound and of extracted teeth and the opportunity for histologic examination of the liver as a result of exploratory laparotomy.

The occurrence of xanthomatous changes in the scars recalled attention to the fact that xanthomatous changes can involve a remarkably wide range of tissue forms besides connective tissue cells, e. g., epithelium, muscles, nerves,[8] benign tumors,[7] sarcoma and carcinoma. It is the duty of the physician to attempt to remove the disguise which the xanthomatous change may be placing over otherwise recognizable clinical complexes. The common ground occupied by Christian-Schüller's disease and multiple myeloma in particular is emphasized, and a plea is made for attention to the possible masquerade not only of reticuloendothelial dyscrasia, so-called, but of such entities as tuberculosis and syphilis, under the guise of xanthoma.

ERYTHROBLASTOSIS FOETALIS

A STUDY OF ITS MODE OF INHERITANCE

MADGE THURLOW MACKLIN, M.D.
LONDON, CANADA

Members of the medical profession have recognized for many years that fatal jaundice of the new-born tends to occur in more than 1 child in a family and that it affects a large percentage of the offspring. Some twenty years ago two laws were formulated with respect to its appearance in a family (Abels [1]), both of which are incorrect. One was that it affected all the children in a family if it affected any and the other that it tended to decrease in intensity from the first to the last child.

For half a century, at least, physicians have been recording instances of the interesting fetal condition known variously as universal edema of the fetus, hydrops foetalis or anasarca of the new-born. Although in some families in which this condition occurred it affected more than 1 child, the familial tendency is not nearly so marked as that of icterus gravis neonatorum.

Recently, a type of congenital anemia has been described in which anemia is profound, the number of nucleated red blood cells and reticulocytes far exceeds the normal, there is no increase in the fragility of the red cells, the spleen and liver are large and splenectomy does not improve, or at least does not permanently improve, the condition. The various organs of the body not ordinarily concerned in hematopoiesis after birth show marked proliferation of the red cells and immature forms of white cells.

Examination of the tissues of children who have died of fatal jaundice of the new-born or of hydrops has revealed that the pathologic picture is the same as that in congenital anemia. The last-named condition was termed erythroblastosis foetalis by Rautmann,[2] who first described it in connection with hydrops, and has been called a condition in which the fetal tendency to manufacture an excess of red blood cells to compensate for its environment of deficient oxygen is carried over into postnatal life. The centers of hematopoiesis that were active in prenatal

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Read before the pediatric section of the Toronto Academy of Medicine on March 19, 1936.

1. Abels, H.: Familial Nature of Jaundice in the Newly Born, Med. Klin. **11**:1307, 1915; abstr., J. A. M. A. **61**:540 (Feb. 12) 1916.

2. Rautmann, H.: Congenital Hydrops, Beitr. z. path. Anat. u. z. allg. Path. **54**:332, 1912.

existence retain their hematopoietic propensities, and the body destroys them in large quantities as they are manufactured. Hence jaundice, anemia and toxemia occur, which result in death in the majority of instances. It is difficult to understand just how this condition produces the edema of the tissues and the large amounts of fluid in the pleural, pericardial and peritoneal cavities and in the placenta which characterize hydrops foetalis. Capon,[3] who studied the maternal history in cases of hydrops, came to the conclusion that there were no constant pathognomonic features which might explain this condition in the fetus. In his opinion the sequence of events is as follows: An overgrowth of intravillous connective tissue, which is out of proportion to the increase in the epithelial surfaces of the villi, damages the nutrition of the fetus in two ways. It causes a compression of the intravillous vessels, and it makes for less absorptive surface in comparison with the bulk of the tissue. The fetus tries to compensate for the compression of the vessels by raising the blood pressure and by increasing the production of blood. Cardiac hypertrophy results. The nutrition remains impaired, and the result is an exudation of fluid into the tissue spaces and serous cavities.

The historical aspects of the subject of erythroblastosis foetalis have been well covered by Capon,[3] Baty and his associates,[4] Andrews and Miller,[5] Diamond and his co-workers[6] and Hawksley and Lightwood[7] the first and the last references being particularly full, and will not be dealt with here.

SCOPE OF THIS STUDY

Several questions have arisen, and it is the purpose of this study to analyze some of them. Each of the three conditions, fatal icterus of the new-born, hydrops foetalis and congenital anemia, has been reported as having occurred in several siblings. Does this mean that the conditions are hereditary? If they have the same pathologic basis, have they the same hereditary basis? That is, if icterus has appeared in 1 child in a family, is the next child affected just as likely to show hydrops or anemia as it is to show icterus? Or is it more likely to show icterus than either of the other two conditions? In the first case, one might assume

3. Capon, N. B.: General Edema of the Fetus, J. Obst. & Gynaec. Brit. Emp. **29**:239, 1922.

4. Baty, J. M.; Blackfan, K. D., and Diamond, L. K.: Blood Studies in Infants and in Children, Am. J. Dis. Child. **43**:667 (March) 1932.

5. Andrews, H. S., and Miller, A. J.: Erythroblastosis in the New-Born, Am. J. Dis. Child. **50**:673 (Sept.) 1935.

6. Diamond, L. K.; Blackfan, K. D., and Baty, J. M.: Erythroblastosis Fetalis and Its Association with Universal Edema of the Fetus, Icterus Neonatorum and Congenital Anemia of the New Born, J. Pediat. **1**:269, 1932.

7. Hawksley, J. C., and Lightwood, R.: A Contribution to the Study of Erythroblastosis: Icterus Gravis Neonatorum, Quart. J. Med. **3**:155, 1934.

that hydrops, icterus and anemia were identical genetically; in the latter, one would conclude that they were not identical but related. Is there evidence that the three conditions are due to a more deep-seated cause than mere inability of the fetus to discard its fetal habits of blood formation?

MATERIAL USED

These questions have been taken up, and some of the cases reported in the literature have been analyzed. Not all the case reports in the literature were available, but a sufficiently large series was collected to be statistically significant. In some of the cases cited the condition was not verified by histologic examination of the blood or tissues. Hence their inclusion might be questioned.

It may be that in some cases the hydrops was not erythroblastotic. In most cases in which histologic examination is performed, however, the condition seems to fall into this category. It may be assumed, therefore, that in the earlier cases it would have belonged there also. With respect to fatal jaundice of the new-born, one must consider at least two types: that which arises in the presence of bile ducts with lumens, which is not obstructive, and that which arises because of the absence of bile ducts. The former type is described as erythroblastosis foetalis. Since by no means all the infants reported in the literature as having had fatal icterus of the new-born were examined at autopsy so that it might be determined whether the bile ducts were present and, if so, if they were patent and whether there was evidence of abnormal hematopoiesis, many cases would have to be excluded from this study if histologic evidence of erythroblastosis were demanded as a criterion. Several features helped to convince me that in the cases which I included the condition was not due to impervious bile ducts and was really of the erythroblastotic type. I excluded all cases in which it was stated that at autopsy atresia of the bile ducts had been found and also all cases in which the patient was said to have had white stools from birth. Some of the latter may have been instances of erythroblastosis, since in some cases definitely proved to be of this class the stools were white. This was due apparently to the fact that the swollen liver cords so pressed on the bile ducts as to prevent drainage or to the unusual viscosity of the bile. Also, all cases were excluded in which the jaundice had lasted for more than two weeks. The majority of patients with erythroblastotic jaundice either die in the first two weeks or gradually recover. The child with jaundice due to atretic bile ducts lives for a longer period, for weeks or even months, with the jaundice gradually deepening. It is admitted that the criteria used to distinguish erythroblastosis are not infallible, but it is felt that the majority of cases included here were really examples of erythroblastosis.

Having described the type of cases used in this study, I shall consider the hereditary nature and the mode of inheritance of the three conditions which are now included in the category of erythroblastosis, icterus, hydrops foetalis and congenital anemia, and shall then deal with the three as if they were the same disease genetically as they have been claimed to be pathologically. The evidence for the hereditary nature of each syndrome will be examined under the following headings: (1) the occurrence of the condition in twins, (2) the frequency of consanguineous marriages of the parents of affected children, (3) statistical analysis of data to determine whether the theory that the condition is

due to a recessive or a dominant gene substitution is tenable, (4) the interpretation of the numerous instances of miscarriage and stillbirths in affected families as evidence of erythroblastosis in the fetus and (5) the practical applications of the study.

ICTERUS NEONATORUM

In dealing with jaundice of the new-born due to an abnormal factor in the production of blood, an attempt will be made to determine (1) whether the condition is hereditary and (2) if it is hereditary its mode of transmission.

Twins.—When one is investigating the probable influence of heredity in the determination of a trait, the study of its occurrence in twins is of value provided the records give adequate information. Unfortunately, such information is not included in the records dealing with icterus neonatorum in 1 or both members of a pair of twins. For the information to be valuable, the sex of both twins, whether or not both are affected, should be given. If the twins are of the same sex, some statement should be given concerning the probability of their being monozygotic or dizygotic. Similarity or dissimilarity in features and coloring and also the condition of the membranes should be noted. In a large series of cases in which both twins are affected, one should find that on the average there is 1 pair of girl twins to 1 pair of boy twins to 1 pair of mixed twins if heredity is playing no part in the production of the icterus. If, however, the proportion of twins of the same sex is much in excess of two-thirds and the proportion of mixed twins considerably below one-third, then one has good evidence that heredity is playing an important part in the causation of the icterus. In a group of twins in which 1 twin only is affected, one should find the same ratio, 1 pair of girls to 1 pair of boys to 1 pair of mixed twins if heredity is not the explanation. If, however, one finds that twins of the same sex constitute only one half instead of two thirds of the series and mixed twins the other half, one has again good evidence that heredity is a determining factor. The larger the series the more significant are the ratios.

In the reported cases of icterus neonatorum, the condition occurred in 7 pairs of twins. In 4 pairs both twins were affected, but nothing was said as to their sex. In 1 pair both twins were affected and both were girls, but nothing was said as to their being monozygotic or dizygotic. In 1 pair of twins, 1 twin died at birth, without having had time to acquire jaundice, and the other twin lived to die of jaundice at the age of 2 or 3 days. The seventh pair of twins was made up of an icteric girl and a stillborn hydropic boy. Thus one gets nothing of real value from a study of this series to settle the question of the hereditary nature of icterus.

Familial Cases of Icterus.—One may turn to the published records of icterus neonatorum in 1 or more children of a family to ascertain if any information as to the rôle of heredity in the disease can be gained. Since practically all the cases reported were in children whose parents were both normal and had never had icterus, the condition has been called familial by physicians to distinguish it from inherited conditions, which pass from parent to child in a direct line of descent. Abt [8] said that heredity plays no rôle in causing icterus gravis neonatorum. Familial conditions are usually inherited according to the recessive mode of transmission, by which, for the most part, unaffected parents have one or more affected offspring. Is the mode of inheritance of icterus neonatorum of the recessive type? If it is, one should find in a large series of cases two relationships, which characterize families in whom a relatively rare recessive disease occurs. First, there should be more consanguineous marriages than there are in the general population. Second, in the large families the number of affected children should be about 25 per cent of the total number of offspring and in the smaller families the percentage should be higher, and by appropriate mathematical formulas, the number of children affected could be determined. These two relationships I tried to find in the series of families with icterus neonatorum.

Consanguineous Marriages: In the 134 families described in the literature in which icterus neonatorum occurred, there was but 1 instance in which parents were said to be related (Hawksley and Lightwood [7]). This is an incidence of 0.74 per cent, while that of marriages of cousins in the general population is said to be about 0.2 per cent (Baur, Fischer and Lenz [9]). This marriage of cousins was probably not responsible for the appearance of icterus in the family, however, for when one examines the rest of the family history one finds that the father of the icteric child had had a brother and 2 sisters die of icterus at the ages of 6, 12 and 2 days, respectively, although his parents were not related. Therefore, one must be cautious about attributing the appearance of icterus in his child to the fact that he had married a first cousin. Although the incidence of marriages of cousins in this series is three times that found in the general population, it is lower than that found in connection with other recessive diseases, which is from fifty to one hundred times as high as that in the general population. One must remember, of course, that this is the minimal incidence of marriages of cousins for this series, since in cases in which a relationship between

8. Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 3, p. 646.

9. Baur, E.; Fischer, E., and Lenz, F.: Human Heredity, ed. 3, New York, The Macmillan Company, 1931.

the parents was not mentioned the omission may have been due to the fact that the physician found the parents not to be related and regarded such negative evidence as worthless or to the fact that the physician failed to inquire concerning this point.

Statistical Analysis: One may then examine the families for which there is a complete record of all the pregnancies and in which some of the children were affected with icterus. These records may give a detailed account of all the pregnancies, or they may merely say that 3 of 5 children had icterus without stating whether the 2 unaffected children were normal and lived, were stillborn or were premature. All these families are listed in table 1, the number of families having 1, 2, 3 or more children being shown in the second column. For the families of each size the following information is given: the total number of children, in the third column; the total number of affected children, in the fourth; the number who would be expected to be affected, if the icterus was due to a recessive factor, in the fifth, and the number who would be expected to be affected if the icterus was due to a dominant factor, in the sixth.

Comparison of columns 4 and 5 shows that with the exception of the 1 child families, in which, of course, all the children had to be affected if the family was to be included in the table, the number actually affected is higher than the number expected to be affected if the disease is due to a recessive factor. The numbers in column 6 approximate the actual numbers of affected children much more closely. The total number of affected children is 394, or 62.3 per cent of the total. The total number of affected children in column 5 is 219.9, and in column 6, 344.8. The average number of affected children per family for the series is 2.9 ± 0.14. The average for column 5 is 1.64, and for column 6, 2.57. The difference between 2.9 and 2.57 is 0.33, which is less than two and one-half times the probable error of 0.14. An analysis of this table, then, indicates that although icterus neonatorum does occur in children whose parents are not affected, it is not inherited as if dependent on a recessive factor, for the number of affected children is far too great and approximates the number of children who would be affected if a dominant factor was involved.

That the parents were unaffected suggests that the condition occurs as a dominant mutation in the families in which children with fatal icterus are born. The mutation may occur in the germ plasm of either parent and may cause in the offspring the appearance of the character which the parent did not possess. Being dominant, it is able to appear in the offspring when only 1 of the parents transmits it, and it tends to appear in 50 per cent of the offspring. If this explanation, that icterus neonatorum is due to a dominant mutation, is correct, it explains (1) why the incidence of marriages of cousins among the parents of

the affected children is so low, (2) why unaffected parents may have affected children and (3) why the number of affected children is so much in excess of 25 per cent, the percentage expected when hybrid parents produce a child with a condition dependent on recessive factors. That the condition almost always proves fatal explains why one finds no long pedigrees which show the character descending from parent to child, as one does with most dominant characters. It recurs in the population only as the germ plasm of some person undergoes the appropriate mutation.

TABLE 1.—*Data on Families Affected by Severe Jaundice* *

Number of Children in Family	Number of Families	Total Number of Children	Total Number Affected	Number Affected, R†	Number Affected, D‡
1	7	7	7	7.0	7.0
2	25	50	32	28.5	33.3
3	17	51	26	22.0	29.1
4	23	92	58	33.6	49.0
5	20	100	62	32.7	51.6
6	13	78	37	23.7	39.6
7	4	28	15	8.0	14.1
8	8	64	36	17.7	32.1
9	9	81	46	21.8	40.5
10	4	40	30	10.6	20.0
11	1	11	10	2.8	5.5
15	2	30	27	7.5	15.0
16	1	16	8	4.0	8.0
Total	134	648	394	219.9	344.8

Average number of affected children per family = 2.9 ± 0.14
Average number of affected children per family, column 5 = 1.64
Average number of affected children per family, column 6 = 2.57

* All miscarriages and stillbirths were omitted when the total number of children in the family was computed, and all children in whom severe jaundice developed were included in the affected children.

† In this and the following tables R indicates the theoretical number of affected children if the condition is inherited and dependent on a single recessive gene substitution.

‡ In this and the following tables D indicates the theoretical number of affected children if the condition is inherited and dependent on a dominant mutation in the germ plasm of one of the parents.

At least 2 instances of parents having been affected are on record. In each case the mother had had the severe type of jaundice in infancy but had finally recovered. Half of her children had fatal jaundice of the new-born, and half were normal (Hichens [10] and Thomson [11]). There are also 2 instances in which the parents of the affected children were normal themselves but had had affected siblings (Hawskley [7] and Taylor [12]). If one conceives of the diseases as dependent on a dominant mutation occurring in the germ plasm of 1 of the parents, one sees how the tendency for the mutation to occur in that strain may be hereditary also. Thus, a woman may give birth to several children who die of

10. Hichens, P. S.: Cases of Familial Jaundice, Proc. Roy. Soc. Med. **6**:197, 1913.

11. Thomson, T. R.: Congenital Family Jaundice, Brit. M. J. **1**:72, 1925.

12. Taylor, W. M.: Hereditary Jaundice, Brit. M. J. **1**:1127, 1925.

jaundice; she may also give birth to several children who have not inherited the mutation itself but have inherited the tendency to produce the mutation. Icterus neonatorum would then appear in an indirect line of inheritance and yet would be due to a dominant mutation.

It might also be that the mutations are not always the same but that the germ plasm of a certain strain is unstable and liable to produce mutations of different varieties. This might be the explanation of the family history reported by Duguid.[13] He related the history of 2 sisters, both of whom were normal. One had a daughter who gave birth to a child with imperforate anus; the other had a daughter who had a child with spina bifida and a son who had 4 children, 2 of whom died of fatal jaundice. Whether this family had a tendency toward mutations which resulted in these three deformities or whether their occurrence was a coincidence, it is impossible, of course, to say.

When I come to the discussion of hydrops, I shall again mention a family history which is suggestive of the theory that erythroblastosis foetalis is due to a dominant mutation.

For table 1, the method of using the family history was to include all children who had had severe icterus, whether they had died or not, among the affected children and to exclude from the total number of children in the family all those who did not come to term or died at birth. Thus, only the children who survived long enough to become icteric were included. There were slightly more affected children than would be expected even on the basis that icterus is due to a dominant mutation. It was felt that perhaps some of the children listed as affected should not have been so included, having had not grave jaundice but merely physiologic icterus. For this reason the histories were reassembled, and only children who had actually died of the condition were included in the list of affected children. These data are in table 2. The total number of affected children was 315, while the number who would be expected to be affected if the condition was due to a dominant mutation was 312.5. The number expected to be affected if the condition was due to a recessive factor was 196.8. The average number of affected children per family was 2.7 ± 0.13. The average for column 6 was 2.67, and for column 5, 1.68. The difference between the actual value, 2.7, and the theoretical value, 2.67, is 0.03, which is less than one fourth of the probable error. This, again, supports the theory that icterus neonatorum is dependent on a dominant factor which by its nature must be a mutation in these families.

An objection might well be brought up here that certainly has some validity. The reason for there being such a large number of affected

13. Duguid, W. R.: A Series of Cases of Icterus Neonatorum, Brit. M. J. **1**:319, 1906.

children in the families reported on might well be the selectivity exercised by physicians in making their reports. It is much more spectacular when 14 or 15 children die of icterus than when 1 or 2 die of it, in a family of 15. The history of the first situation would almost certainly be recorded, while that of the latter might or might not be. On the other hand, for the small families, in which there is no such spectacular opportunity for large numbers to be affected, one finds that the actual values, in column 4, and the theoretical values, in column 6, agree even better than they do for the large families. In 2 child families 28 children were affected, and 28 were expected to be affected. In 3 child families the two values were 18 and 20.5, and in 4 child families they were 46 and 49.

TABLE 2.—*Data on Families Affected by Fatal Jaundice of the New-Born**

Number of Children in Family	Number of Families	Total Number of Children	Total Number Affected	Number Affected, R	Number Affected, D
1	4	4	4	4.0	4.0
2	21	42	28	24.0	28.0
3	12	36	18	15.5	20.5
4	23	92	46	33.6	49.0
5	18	90	54	29.4	46.4
6	10	60	26	18.2	30.5
7	5	35	15	10.0	17.6
8	8	64	26	17.7	32.0
9	8	72	36	19.4	36.0
10	4	40	23	10.6	20.0
11	1	11	10	2.8	5.5
15	2	30	21	7.6	15.0
16	1	16	8	4.0	8.0
Total	117	592	315	196.8	312.5

Average number of affected children per family = 2.7 ± 0.13
Average number of affected children per family, column 5 = 1.68
Average number of affected children per family, column 6 = 2.67

* All miscarriages and stillbirths were omitted when the total number of children in the family was computed, and only children who died of jaundice were included in the affected children.

From evidence presented in tables 1 and 2 and from the study of consanguineous marriages, it appears probable that fatal jaundice of the new-born is due to a dominant mutation occurring in the germ plasm of one of the parents. Although it is inherited as a dominant character, one does not find long pedigrees showing the direct line of descent, for the disease usually ends in the death of the affected child within a few days of birth.

GENERAL EDEMA OF THE FETUS

If icterus neonatorum and edema of the fetus are expressions of the same pathologic process, one will expect to find not only similar pathologic pictures but interchangeability in the appearance of the two conditions in a single family. One child will have icterus, the next edema and so on. Moreover, one will expect to find general edema of

the fetus occurring as a dominant mutation and not as a condition dependent on recessive factors. Before the data relative to the type of inheritance are analyzed, the evidence from the records of twins and of consanguineous marriages will be reviewed.

Consanguineous Marriages.—In 123 families in which children were born with general edema, there was a single instance in which the parents were related. This low incidence of marriages of cousins does not support the idea that edema of the fetus is due to a recessive factor.

Twins.—With respect to twins, no instances from the literature were examined in which both twins showed edema. In 9 instances 1 twin was edematous. In 2 the affected twin was a boy and the normal twin was a girl. In 3 both twins were girls, with 1 affected. In 2 the

TABLE 3.—*Data on Families' Hydrops Foetalis* *

Number of Children in Family	Number of Families	Total Number of Children	Total Number Affected	Number Affected, R
1	12	12	12	12.0
2	18	36	21	20.0
3	17	51	17	22.0
4	19	76	24	27.7
5	15	75	17	24.5
6	11	66	11	20.0
7	12	84	13	24.1
8	1	8	1	2.2
9	7	63	9	17.0
11	3	33	3	8.6
12	2	24	7	6.2
13	1	13	1	3.3
Total	118	541	136	187.6

* All miscarriages and stillbirths were omitted when the total number of children was computed, and only children who showed general edema were listed as affected. The theoretical number D was not computed because the theoretical number R was far too high.

sex of the twins was not mentioned. In 1 the twins were boys, with 1 affected and 1 normal. In 1 there was a hydropic boy and an icteric girl. That 1 of the twins was affected and the other was normal in 8 of 9 cases at least argues against the responsibility of some factor in the maternal history for the edema in the fetus. This is in agreement with Capon's finding that there was no constant pathognomonic feature in the maternal history which could be regarded as a causative factor. If some extraneous condition outside the make-up of the twin himself were responsible, both twins would have been affected, since both are affected equally by changes in the intra-uterine environment.

Statistical Analysis.—When one sets forth the data dealing with the number of affected children in the various-sized families, as has been done in table 3, one gets some unexpected results. As in the first two tables, all miscarriages and stillbirths were omitted from the records, and only the offspring born alive at term were counted in the number of

children in the family, and only those affected with edema were listed as affected. Contrary to the findings in the case of icterus, one sees that too few children were affected for the condition to be considered even as recessive. Only 136 children were affected, and 187.6 should have been affected if the condition was dependent on a single recessive gene substitution. This value was so much higher than that actually found that the number expected to be affected if the condition was due to a dominant factor was not calculated, for that would have been still higher. Is it probable, then, that general edema of the fetus, while pathologically like icterus, is genetically quite different?

These two conditions are not infrequently found in the same family, so that there is good ground for believing them connected in some way other than by their mere pathologic manifestations. Moreover, edema of the fetus, although occurring much less frequently in several members of a family, is found in siblings with sufficient frequency to make one think that an inherent quality in the family affected causes the condition to reappear. Thus, 118 families had 136 cases of hydrops. In addition to these families, which are listed in table 3, there were others not included because the total number of children was not given in the records. There were 3 families with 2 hydropic children, 1 with 3 and 1 with 4. For 123 families there were 149 cases of edema, an average of 1.21 cases to a family.

The combination of hydrops with icterus was not infrequent. In 14 of 123 families, or a little over 11 per cent, the two conditions were found together. There were 7 families with 1 hydropic child and 1 icteric child, 3 with 1 hydropic and 2 icteric children, 1 with 1 hydropic and 3 icteric children, and 1 with 1 hydropic and 4 icteric children. There were 2 families in which 2 children had hydrops and 1 had icterus.

Although it appears from the analysis of the data that hydrops of the fetus and icterus neonatorum are not manifestations of the same disease, it is evident that they are closely related. Two tenable explanations occur.

Both conditions may be dependent on a single inherited factor which calls for abnormal production of blood in the fetus. Icterus may be the result of that mutation in unmodified form. Hydrops may be due to the same mutation, to which has been added a modifying factor, resident either in the same or in another chromosome pair, which leaves the blood picture the same but alters the clinical picture from one of jaundice to one of extreme edema. With this genetic basis, one might expect that more families would exhibit icterus than hydrops and that the number of children in a family affected with icterus would be much higher than the number affected with hydrops, since the latter depends

on an additional factor. One might also expect that in some families the two conditions would be found, the mutation in unmodified form having occurred in some children and an additional mutation causing the development of hydrops in others.

On the other hand, one might conceive of icterus neonatorum and hydrops being dependent on mutations which occurred in the same chromosome and at the same location in the chromosome, in other words, which were multiple allelomorphs of the normal condition. Such an explanation would account for the appearance of edema in one child of the family and of icterus in another, for the germ plasm might mutate first in one way and then in another. It would also account for a tendency to mutate in the same way most often and thus explain the fact that in 89 per cent of the families icterus or edema occurred alone.

If these two conditions are multiple allelomorphs, it may well be that they exhibit varying degrees of dominance to the normal allelomorph from which they mutated. Icterus might be dominant over the normal, while hydrops might exhibit a degree of dominance so much less that it would be recessive to the normal. At this point it is necessary to mention one of the characteristics of the families in which hydrops has occurred and to offer evidence that hydrops may be a dominant mutation, as is icterus.

In families in which hydropic children have been born, there is almost always a history of an undue number of miscarriages, premature births, stillbirths, births of macerated fetuses and similar anomalies. In some families, there have been from 12 to 14 pregnancies, with only 1 living normal child as a result. All the rest of the pregnancies have terminated in miscarriage or stillbirth. May it be that these prematurely ending pregnancies terminated early because the fetus had inherited the factor for hydrops and had the condition in so extreme a form as to cause the pregnancy to end too early for the hydrops to be recognized? If this is so, then one should include when computing the number of children in the family and the number of affected children all the miscarriages and stillbirths.

This has been done, and the data appear in table 4. There were 237 affected children in 98 families, with an average of 2.4 ± 0.15 affected children to a family. If this disease was due to a dominant mutation which when severe caused some pregnancies to terminate early and when less severe caused the fetus to exhibit hydrops, then one should expect 244.9 children to be affected in these families, with an average of 2.5 affected children in a family. The difference between 2.4 and 2.5 is only 0.1, which is less than the probable error. This analysis suggests that hydrops is a dominant mutation and that it is of such severity in some instances as not to let the fetus grow to the point at which edema

is evident. This theory can be put to the test by examination of all the products of conception in families in which hydrops foetalis has occurred for the erythroblastotic tendencies which are present in cases in which edema of the fetus develops. Such examination is urged on physicians who deal with families affected by hydrops.

A record furnished by Ballantyne [14] supports the idea that hydrops is due to a mutation of the germ plasm, that it is not dependent on maternal conditions and that miscarriages and stillbirths in families affected by hydrops are to be regarded, in part at least, as evidence of the disease rather than entirely as evidence of the action of outside forces.

TABLE 4.—*Data on Families Affected by Hydrops Foetalis, Including Data on All Pregnancies* *

Number of Children in Family	Number of Families	Total Number of Children	Total Number Affected	Number Affected, R	Number Affected, D
1	9	9	9	9.0	9.0
2	18	36	24	20.5	24.0
3	14	42	17	18.1	24.0
4	13	52	26	19.0	27.7
5	12	60	35	19.6	31.0
6	12	72	27	21.9	36.5
7	6	42	21	12.0	21.2
8	2	16	11	4.4	8.0
9	4	36	9	9.7	18.0
10	2	20	17	5.3	10.0
11	1	11	1	2.8	5.5
12	5	60	40	15.5	30.0
Total	98	456	237	157.8	244.9

Average number of affected children per family = 2.4 ± 0.15
Average number of affected children per family, column 5 = 1.6
Average number of affected children per family, column 6 = 2.5†

* All pregnancies were counted when the total number of children was computed, and all stillbirths, miscarriages and cases of erythroblastosis foetalis were considered when the number of affected children was computed.

† This figure is almost identical with that for the average number of children actually affected, the difference between the two being only two thirds of the probable error.

The fathers of the hydropic offspring were brothers, and it was not mentioned that the wives were related either to each other or to the husbands. Thus the defect seemed to come from the male parent. Both fathers were pale and waxy looking. (It may be that they had suffered from congenital anemia, another erythroblastotic disease.) The wife of one brother had 12 pregnancies, of which the first 2 resulted in healthy children. The next 5 ended in stillbirths, the eighth in a stillbirth with an extensively diseased placenta, the ninth and tenth in edematous fetuses, with edematous placentas, the eleventh in a premature stillbirth at 7 months, and the twelfth in a 6 month fetus, with edema of the fetus and of the placenta. The wife of the second brother had 6 abortions. The seventh pregnancy resulted in an edematous fetus and the eighth in the stillbirth of a child about whose condition nothing was said.

14. Ballantyne, J. W.: General Dropsy of the Fetus, Edinburgh M. J. **38**:57, 1892.

These cases are comprehensible if one considers hydrops as due to a mutation and the miscarriages as evidences of hydropic fetuses discarded before the condition was sufficiently advanced for the physician to recognize it.

Before going on to an analysis of congenital anemia (which is the third member of the group showing erythroblastosis histologically, although it reveals a widely differing clinical syndrome), I shall analyze further the idea that in families affected by icterus and hydrops the miscarriages and similar anomalies, or at least some of them, are caused by the inheritance of the factor for erythroblastosis by offspring who cannot survive long enough in the prenatal period for the full clinical syndrome to develop. Some of the pregnancies terminating early ended for reasons other than the foregoing. In many families in which there is no evidence of abnormal formation of blood in the fetus, there are miscarriages. But so characteristic is the history of miscarriages and stillbirths in families affected by icterus and hydrops that the idea became strong that a certain percentage of prematurely ending pregnancies were evidence of the disease itself.

I tried to test this idea out. I reasoned in this way: Edema of the fetus is more fatal to the fetus than is jaundice, for with edema the child does not survive the period of birth, while with jaundice the child is born alive but cannot survive the period after birth. If the two diseases are expressions of the same underlying condition, with one much more severe than the other, and if the products of the miscarriages and stillbirths in these families are to be regarded in part as defective offspring aborted early because of the unusual severity of the condition in them, one will find that in families in which edema of the fetus has appeared the number of miscarriages is much higher in proportion to the total number of pregnancies than it is in families affected by icterus. More of the defective children will be eliminated before birth in hydropic families; hence fewer will come to the point of having recognizable hydrops. In the families in which icterus has appeared but in which there are no cases of hydrops, one will expect the number of miscarriages to be less and the number of children surviving to the time of birth, in whom jaundice may develop, to be higher.

If one considers only the families for which complete histories of the pregnancies are given, one obtains the data set forth in table 5. There were 83 families with hydropic infants, with a total of 395 pregnancies, an average of 4.8 pregnancies per family. One hundred, or 25.2 per cent, of these pregnancies resulted in miscarriage or stillbirth, and 119, or 30.1 per cent, in the birth of a child in whom hydrops foetalis developed. In the 115 families affected by icterus there were 635 pregnancies, or an average of 5.5 pregnancies per family. Of these, 76, or 11.9 per cent, resulted in miscarriage or stillbirth, and 369, or

58.1 per cent, in the birth of a child affected by icterus. Thus, although the percentage of pregnancies which resulted abnormally was smaller in the hydropic families (55.3 per cent of the total) than in the icteric families (70 per cent of the total), more pregnancies were terminated early (25.2 per cent, as against 11.9 per cent). The smaller total percentage of abnormal pregnancies in the hydropic families as compared with that in the icteric families (55.3 per cent, as against 70 per cent) might be explained on the basis that in families with icterus the number of children who survive until birth and can thus show the defect is much greater than it is in families with hydrops and that the tendency to report cases of large families with many children affected is greater than that to report cases of large families with only a few

TABLE 5.—*Data on Families for Which the History of All Pregnancies Is Available* *

	Number of Families	Number of Pregnancies	Average Number of Children per Family	Number of Miscarriages and Stillbirths	Percentage of Pregnancies Ending in Miscarriage or Stillbirth	Number of Children Affected	Percentage of All Fetuses and Children Showing Defect	Pregnancies Resulting in Defective Child or Miscarriage
Hydrops foetalis...	83	395	4.8	100	25.2	119	30.1	55.3
Icterus neonatorum	115	635	5.5	76	11.9	369	58.1	70.0
Congenital anemia.	61	227	3.7	18	8.0	88	38.7	46.7

* In the families listed under hydrops are included all families in which 1 child at least had hydrops foetalis. Under icterus are listed families in which 1 child at least had icterus but in which none had hydrops. Under congenital anemia are listed all families in which only anemia was reported. The families are thus divided into three groups of decreasing intensity as far as the disease is concerned.

children affected. Thus, the series of icteric families would be overweighted, since many children may be affected in a family.

This study of the number of miscarriages and stillbirths in families affected by hydrops and icterus does not of course prove that the fetus or infant had erythroblastosis. Only examination of the tissues of all the products of conception in icteric and hydropic families can settle that question. But the data do suggest that here is a fruitful line of study, and they will have served their purpose if they direct the attention of the obstetrician and the pediatrician to the necessity of examining adequately all the products of conception that come to an early death in such families.

CONGENITAL ANEMIA

In congenital anemia, erythroblastosis foetalis is also present. Does it appear to be inherited; if so, does its mode of inheritance agree with that of icterus and is it the third possible allelomorph in this series of departures from the normal? As with the other two conditions discussed, what information may be gained from a study of twins?

Twins.—Seven pairs of twins have been reported on in which 1 or both twins were affected. In 2 pairs with the sex not mentioned both were affected, and in 1 pair with the sex not mentioned 1 was affected. Their cases may be dismissed as giving practically no information. In 1 pair of girl twins and 1 pair of boy twins both twins were affected. In 1 pair of girl twins 1 twin was affected, and in 1 pair of twins with a boy affected the sex of the normal twin was not given. If the physician who reported these cases had realized the genetic value of data on twins and had given full details as to sex and as to whether the twins were monozygotic, these data would have been of value. As reported, they are practically worthless genetically except as an indication that maternal influences are not likely to be of importance, since half of the pairs of twins had 1 unaffected member as well as 1 affected member.

Consanguineous Marriages.—No statement was made as to the presence or absence of marriages of cousins.

Racial Distribution.—A racial factor seems to be at work in the production of congenital anemia. In practically all the cases which have been reported and in which the nationality of the parents was mentioned, the parents were born in countries bordering on the Mediterranean; for the most part, they were either Greek or Italian. It thus appears that a mutation has arisen in the germ plasm of these persons to produce a type of erythroblastosis foetalis that is sufficiently mild for the affected child to survive long enough to show the anemia, which undoubtedly must be present also in fatal jaundice, with its marked destruction of the blood. The jaundice probably masks the anemia if it is present, and the child usually dies before the anemia has a chance to become profound. Thus although anemia has been found in children with hydrops and in children with jaundice, children who have anemia as the most prominent symptom must have such a mild type that it permits them to live to the point of showing it.

Just as hydrops and jaundice were found together in about 11 per cent of icteric families, so anemia is recorded as occurring in families which show the other two conditions. One family had 1 icteric and 1 anemic child; 1 had 1 icteric and 2 anemic children; 2 had 1 icteric and 3 anemic children, and 1 had 2 hydropic children and 1 who was anemic. There were 3 instances of jaundice and edema in the same infant, 19 of jaundice and anemia, 1 of anemia and hydrops and 1 of all three conditions.

Statistical Analysis.—In table 6 are the data for the families with congenital anemia. When only the anemic children in the family are listed as affected, the ratio of affected children to normal children approximates closely that which would be expected if the defect is due to a recessive gene substitution rather than to a dominant gene substitution. There were 267 children in the families, of whom 114 were

affected. If the condition is due to a recessive factor, one would expect 106.2 children to be affected, an almost perfect agreement. If the condition is due to a dominant factor, one would expect 150.4 children to be affected. The average number of affected children per family was 1.5 ± 0.07; if the characteristic is recessive, the average number would be 1.4, and if it is dominant, the figure would be 1.9. The difference between 1.5 and 1.4 is only 1½ times the probable error. This, then, indicates that congenital anemia is due to a recessive gene substitution.

It must be remembered, however, that in these families some children showed icterus and some hydrops and that there were miscarriages and stillbirths, which might be evidence that the disease had severely affected the unborn fetus. When the data are reassembled, as has been

TABLE 6.—*Data on Families Affected by Congenital Anemia**

Number of Children in Family	Number of Families	Total Number of Children	Total Number Affected	Number Affected, R	Number Affected, D
1	12	12	12	12.0	12.0
2	16	32	19	18.3	21.3
3	16	48	19	20.7	27.4
4	11	44	19	14.7	23.4
5	9	45	22	14.7	23.2
6	4	24	7	5.4	12.1
7	3	21	4	6.0	10.5
8	4	32	11	4.4	16.0
9	1	9	1	2.4	4.5
Total	76	267	114	106.2	150.4

Average number of affected children per family = 1.5 ± 0.07
Average number of affected children per family, column 5 = 1.4
Average number of affected children per family, column 6 = 1.9

* Only children born alive were included in the total number of children, and only those affected by anemia were included in the affected children.

done for icterus and hydrops, and all pregnancies are considered when the total number of children is computed and all the children with any form of erythroblastosis, all miscarriages and all stillbirths are considered when the number of affected children is computed, one has the information listed in table 7. Of a total of 926 children, 600 were affected, whereas one would expect the number to be only 490.6 on the dominant gene hypothesis. A smaller number would be expected on the recessive gene theory. Therefore, it appears that the number of affected children is too great to suit the dominant mutation theory. The explanation may be that with the milder form of the condition, the products of miscarriage and stillbirth were not affected with erythroblastosis and that their inclusion, bringing the figure up to 600, made it much higher than it should be. Could one eliminate the miscarriages and stillbirths of which the products were not affected by erythroblastosis one would probably have a much closer approximation of the theoretical and the actual results.

When one looks at table 5, one sees that just as icterus is a milder expression of the disease than hydrops and fewer children were consequently lost before birth in the icteric families, so congenital anemia is a milder form of the condition than icterus, and fewer of the pregnancies resulted in miscarriages. It may be that only in the hydropic families are some of the miscarriages examples of erythroblastosis foetalis. Only examination of the tissues of the fetuses can decide this question.

If one groups all three clinical syndromes together and lists the families, one gets the data given in table 8. Here, again, the prema-

TABLE 7.—*Data on Families Affected by Congenital Anemia, Including Data on All Pregnancies* *

Number of Children in Family	Number of Families	Total Number of Children	Total Number Affected	Number Affected, D
1	8	8	8	8.0
2	32	64	41	42.6
3	24	72	44	41.1
4	32	128	83	68.2
5	24	120	77	61.9
6	20	120	71	60.9
7	7	49	29	24.7
8	13	104	54	52.7
9	6	54	34	27.0
10	6	60	44	30.0
11	2	22	16	11.0
12	3	36	30	18.0
13	2	26	20	13.0
14	1	14	8	7.0
15	2	30	27	15.0
19	1	19	14	9.5
Total	183	926	600	490.6

Average number of affected children per family = 3.28 ± 0.13
Average number of affected children per family, column 5 = 2.7

* All pregnancies were counted when the total number of children was computed, and all children with any type of erythroblastosis and all miscarriages and stillbirths were considered when the number of affected children was computed. The number of affected children is too high in this table and too low in table 6, indicating that some of the miscarriages may have been due to congenital anemia while others were not.

turely ending pregnancies were disregarded in computing both the total number of children and the list of affected children. Of a total of 1,232 children, 608 were affected, while the expectation would be 667.2 according to the dominant gene theory and 439.5 according to the recessive gene theory. The average number of affected children per family was 2.15 ± 0.14, while the average number expected to be affected if the condition is due to a dominant mutation is 2.36. The difference between the two values is 0.21, which is only 1½ times its probable error.

If one rearranges the data, as has been done for each syndrome separately, and includes all the prematurely ending pregnancies in computing both the total number of children and the number affected, one gets the results recorded in table 9. Of 1,244 children, 752 were

TABLE 8.—*Data on Families Affected by Erythroblastosis Foetalis* *

Number of Children in Family	Number of Families	Total Number of Children	Total Number Affected	Number Affected, D	Number Affected, R
1	30	30	30	30.0	30.0
2	49	98	58	65.3	56.0
3	45	135	62	77.0	58.3
4	43	172	93	91.6	62.7
5	39	195	102	100.6	63.7
6	24	144	56	73.1	44.2
7	15	105	29	52.9	30.2
8	11	88	45	44.2	24.3
9	15	135	55	67.5	36.5
10	5	50	40	25.0	13.3
11	2	22	2	11.0	5.7
13	1	13	1	6.5	3.3
15	3	45	35	22.5	11.3
Total	282	1,232	608	667.2	439.5

Average number of affected children per family = 2.15 ± 0.14
Average number of affected children per family, column 5 = 2.36
Average number of affected children per family, column 6 = 1.55

* Erythroblastosis foetalis occurred in the form of congenital anemia, fatal icterus of the new-born or hydrops foetalis. All miscarriages and stillbirths were omitted when the total number of children was computed, and only children affected with one of these three conditions were included among the affected children.

TABLE 9.—*Data on Families Affected by Erythroblastosis Foetalis, Including Data on All Pregnancies* *

Number of Children in Family	Number of Families	Total Number of Children	Total Number Affected	Number Affected, D
1	17	17	17	17.0
2	40	80	53	53.3
3	34	102	53	58.2
4	42	168	102	89.8
5	30	150	88	77.4
6	28	168	98	85.3
7	16	112	56	56.5
8	14	112	60	56.2
9	8	72	33	36.0
10	8	80	61	40.0
11	2	22	16	11.0
12	6	72	51	36.0
13	2	26	20	13.0
14	1	14	8	7.0
15	2	30	27	15.0
19	1	19	14	9.5
Total	251	1,244	752	661.2

Average number of affected children per family = 3 ± 0.17
Average number of affected children per family, column 5 = 2.63 †

* Only families for which a complete record of all miscarriages, stillbirths and affected offspring was available were used. All pregnancies were included when the total number of children was computed, and all pregnancies ending prematurely were considered when the total number of affected children was computed.

† The difference between these two values is only a little more than twice the probable error; hence the data again agree with the theory that erythroblastosis is due to a dominant mutation.

affected, and only 661.2 would be expected to be affected if the condition is due to a dominant factor. The average values for the affected children per family were 3 ± 0.17 and 2.63, respectively. It may well be that some of the children actually affected were omitted in the compiling of table 8 and that the figures in column 4 are too low as compared with those in column 5; while in the compiling of table 9 the reverse may have occurred, some nonaffected children having been included, so that the theoretical value is too low as compared with the actual value, in column 4.

From the analysis of the data it seems reasonable to conclude that although the three conditions, icterus, hydrops foetalis and congenital anemia, show the same pathologic picture, they are not genetically identical but are closely related. The evidence suggests that they may be regarded as three allelomorphs to the normal factor for production of blood in the fetus and that they occur as mutations in the families in which they appear. From the standpoint of the severity of the condition, their order according to decreasing intensity is hydrops, icterus and congenital anemia. From the standpoint of dominance over the normal, the order appears to be icterus, congenital anemia and hydrops. The latter order may not be correct, and histologic examination of the fetuses lost by miscarriage is necessary before the accuracy of the arrangement can definitely be determined.

So far, the matter might seem purely theoretical and of little value to the practitioner of medicine. It has, however, a definite practical application. With the advent of transfusion to combat both icterus and congenital anemia and to enable the victim of these conditions to survive and reproduce, a new problem arises. If these conditions are not hereditary, then one need have no fear of repetition of the disease in the next generation. If they are hereditary and are due to a recessive gene substitution, then, because they are relatively rare, the person who has been affected and has recovered is not likely to pass on his defect to his offspring unless he marries a cousin. Therefore, the advice given by the physician to a patient who desires to know what the chance is, if he has children, of their suffering and perhaps dying of icterus or anemia would be that the chance was fairly remote unless he married a relative. If, on the other hand, the condition is due to a dominant mutation and a patient who recovers has children, half of them will probably contract icterus or anemia no matter whom he marries. The records of the 2 mothers who contracted severe icterus and recovered, only to have half of their children die of the disease, bear this out. The child saved from icterus neonatorum is in danger not only of having cerebral lesions develop owing to injury of the nervous system during the disease, but if the disease is due to a dominant mutation, which idea is strongly supported by analysis of the data, of passing on the defect.

There is a practical application not only in the case of icterus and anemia but in the case of hydrops as well. Although the physician cannot say to a mother that the chances are one in two that she will give birth to a second hydropic offspring if she has given birth to one, he can say that she is not likely to bear a living child and that the chances are at least one in two that she will have a miscarriage or a stillbirth of a hydropic fetus.

As an illustration of the importance of this study to the practitioner in advising his patient, I shall report briefly a case of hydrops foetalis which is being reported elsewhere (C. C. Macklin and others).

A woman who had 2 pregnancies result in normal children, 1 of whom died in infancy, had 4 miscarriages and a stillborn hydropic child. She was desirous of having more children. There was no evidence of syphilis, malposition or other determinable cause to explain the miscarriages. What advice should be given? On the basis of her history and the results of this study, I recommended that she refrain from any more pregnancies, since the chances were one in two that her pregnancy would not give her a viable child.

Is erythroblastosis merely a prolongation of fetal conditions into postnatal life, or is it a more profound disturbance of fetal physiology and morphology? Examination of one hydropic fetus at 6 months showed that even then it had marked alteration in the formation of blood and was not forming red blood cells as does the average fetus of 6 months. Erythroblastosis foetalis is abnormal production of blood even in the early fetal stages and is not merely inability of the fetus to adjust itself rapidly to a high oxygen content in the air after birth.

SUMMARY

Icterus neonatorum of the grave type, hydrops foetalis and congenital anemia have been regarded as the same disease owing to the similar pathologic picture found in all three. They have not been regarded for the most part as evidence of an inherited disease. This study shows the following facts:

1. They are inherited, and genetically they are different although pathologically they may be similar.

2. They are probably multiple allelomorphs to the normal gene or genes for formation of blood in the fetus.

3. Icterus gives evidence of being due to dominant mutations, since a little over 50 per cent of the children in the family are affected when a large series of cases is considered.

4. Hydrops foetalis does not affect half the children in the family but is so constantly associated with a history of miscarriages and stillbirths as to suggest that these anomalies are, in part at least, due to the same inherited factor for hydrops, the condition being so severe

as to cause the early termination of the pregnancy. If this is correct, hydrops foetalis is also due to a dominant mutation.

5. Congenital anemia alone does not affect half the children in the family, but when all the children with erythroblastosis in the families are considered, anemia also appears to be due to a dominant mutation.

6. The mutation for congenital anemia seems to be sharply limited to the races whose home is on the Mediterranean.

7. Strains of germ plasm which produce the mutation for one of these three conditions are able to produce the allelomorphic mutations calling for the other two conditions, as is evidenced by the appearance of icterus and hydrops, of icterus and anemia or of hydrops and anemia in children of the same family.

8. The tendency for only one type of mutation to be produced in a family is stronger than the tendency for several to be produced, as is evidenced by the fact that the majority of families tend to have children who show only one of the three conditions.

9. There are practical applications of this theoretical study of the mode of inheritance of erythroblastosis foetalis. Since transfusion now enables the patient to survive to the reproductive period, there is opportunity for the direct transmission of the defect to offspring, and to 50 per cent of the offspring on the average, if the theory that the conditions are due to dominant mutation is correct. These diseases, which before were relatively rare, being dependent on the chance that mutation might occur in the germ plasm of some parent, will become much more common as patients with them survive to the age of reproduction and pass them on to their children.

10. Although the average affected family does not have more than 1 case of hydrops foetalis occurring, the chances for a mother to produce a viable child are only one in two, since such families have a high percentage of miscarriages and stillbirths, some of which it is suggested are caused by the inheritance of the same factor as that which produces the hydrops, but in such a severe form that the fetus is unable to survive long enough for the picture of hydrops to develop and dies at an early stage.

It is urged that obstetricians who have families in their care in which children are born with icterus, hydrops or congenital anemia examine for evidences of erythroblastosis all products of conception which die before or shortly after birth to determine what percentage, if any, of the anomalies can be attributed to the inheritance of the factor for erythroblastosis and that they report such cases.

It is urged also that in reporting cases of this or any other condition which may possibly be inherited the physician give chronological data concerning the number of pregnancies the mother has had; the end-

result of each; the sex of the offspring, whenever possible; any evidences as to the cause of the miscarriage; for twins, the sex of both and the evidence or lack of it for their monozygosity when both are of the same sex, and, finally, a definite statement as to the consanguinity or lack of it in the parents of the affected children. Thus records which are valuable from the genetic standpoint as well as from the clinical will be available.

Prof. Charles C. Macklin suggested this study after he had made a histologic examination of the tissues in a case of hydrops with erythroblastosis foetalis.

Case Reports

CONGENITAL ABSENCE OF THE RIGHT PULMONARY ARTERY IN A NEW-BORN INFANT

WITH RESULTING NECROSIS OF THE LUNG AND SPONTANEOUS PNEUMOTHORAX

J. FLEEK MILLER, M.D.
NEWARK, OHIO

Seventeen cases of spontaneous pneumothorax of the new-born have been reported, and these cases were collected and reviewed recently by Glaser and Landau.[1] A painstaking search of the literature has failed to yield any reports of cases in which there was a complete absence of the right pulmonary artery.

The cases in which the etiology of the pneumothorax could be discovered fell into three general classes (Willi[2]): (1) those in which the condition was mechanical, or in which artificial respiration or mechanical obstruction by a thymus is supposed to have precipitated the rupture of a normal or emphysematous lung; (2) those in which the condition was infectious, or in which an abscess of the lung had ruptured, and (3) those in which congenital defects of the lung or congenital emphysema acting with or without abnormal mechanical strain resulted in rupture.

In this report, I wish to add one case of spontaneous pneumothorax, making the total number of cases reported eighteen, and also to present a fourth cause for this syndrome: congenital absence of the pulmonary artery to the right lung, with ischemic necrosis of that lung, followed by rupture and consequential pneumothorax.

The patient was seen in the obstetric service of the Newark City Hospital, to which I was called in consultation by Dr. Dale Roth, and was transferred to the pediatric service.

The baby was a boy. I saw him first on the fourth day of his life. The family history showed no syphilis or other congenital disease. The baby was the first living child, the mother having previously had a miscarriage at three months.

He was born normally at term after a fairly easy labor. An episiotomy was done, and the baby was delievered by Scanzoni's maneuver, with the mother

From the pediatric service of the Newark Hospital.

1. Glaser, J., and Landau, D. B.: Pneumothorax of the New-Born, Am. J. Dis. Child. **55**:988-997 (Oct.) 1935.

2. Willi, H.: Schweiz. med. Wchnschr. **64**: 229-233 (March 10) 1934.

under ether anesthesia. While the infant had a good deal of mucus at birth, this was easily removed, and he breathed without the help of mouth to mouth inspiration or any other radical means of resuscitation. He seemed to be well and nursed vigorously.

On the fourth day dyspnea and marked cyanosis suddenly developed, and the temperature rose to 100.6 F.

Examination showed an acutely ill baby, dyspneic and cyanotic. The right side of the chest was tympanitic, with breath sounds absent over it. The borders of the heart could not be made out by percussion, but the heart sounds were loudest in the left axilla. The left side of the chest gave a normal percussion note and normal puerile breath sounds, but there were a few fine crepitant râles at the base of the left lung. A roentgenogram showed tension pneumothorax on the right side, with marked displacement of the mediastinum to the left. The right lung was collapsed and the left lung clear. The white blood cells numbered 27,750 per cubic millimeter, with 84 per cent polymorphonuclear neutrophils, 14 per cent lymphocytes and 2 per cent monocytes.

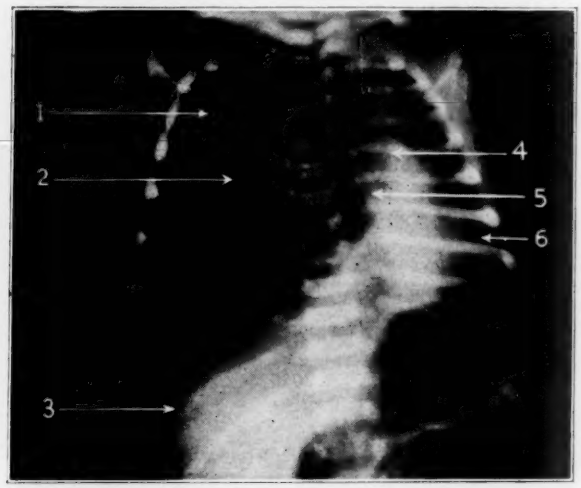

Fig. 1.—Roentgenogram taken on the fifth day of life, showing tension pneumothorax of the right side, with marked displacement of the mediastinum to the left. Even the esophagus, which is visualized, was displaced to the left. The arrows indicate (1) the pneumothorax, (2) the collapsed right lung, (3) the liver, displaced downward, (4) the left border of the pneumothorax, (5) the esophagus and (6) the left border of the heart; the right border of the heart is not visualized.

The infant's chest was tapped. The positive pressure of air was so great that the piston of the syringe was forced up. After 1,500 cc. of air was removed, there seemed to be no diminution in the amount, and when the syringe was removed from the needle, air blew out of the needle on each expiration, showing a valve action on the air entering the pleural cavity. A 10 F. catheter was therefore introduced between the ribs through a trochar and attached to a suction apparatus maintaining a constant negative pressure of 10 cm. of water. The baby's color improved and, with the help of oxygen inhalations, remained fairly good until death occurred, two days later.

Autopsy was performed ten hours post mortem. The pathologic changes were confined to the chest. The mediastinum was displaced to the left, and the right pleural cavity was filled with air and about 5 cc. of bloody fluid. The right lung was completely collapsed and was adherent to the posterior wall of the chest by fibrinous adhesions which were easily broken. The right lung was a dull red, and there was a grossly necrotic grayish sunken area on the anterior surface. A ragged perforation in this area was covered by a flap of necrotic lung tissue, which apparently acted as a valve. This perforation exuded air and saline fluid when they were injected into the right bronchus with a syringe. The heart was displaced to the left but was not enlarged, and the left lung was compressed but fairly well aerated and had a mottled reddish appearance.

The thoracic organs were removed *in toto*. The great vessels from the aorta were normal. No right pulmonary artery could be discovered, not even a vestigial

Fig. 2.—Photograph of the pulmonary artery laid open. The ductus arteriosus has also been opened, to show its size and position. The absence of any vestige of a right pulmonary artery may be noted.

cord. The pulmonary artery was opened and traced into the left lung. No remains or vestiges of a right pulmonary artery were visible from the inside of the artery. The left pulmonary artery was of normal size, 6 mm. in diameter, and the ductus arteriosus, which was patent, was 2 mm. in diameter and 5 mm. in length.

The heart was opened in the usual manner, the incision being made following the line of the flow of the blood. The foramen ovale was seen to be patent and measured 1.3 cm. in diameter. There was no interventricular septal defect, and the valves were normal. The aorta was normally situated and of normal size. Two pulmonary veins entered the left auricle from each lung and were of about equal size, but they were too small to trace grossly.

On microscopic examination the right lung showed varying stages of necrosis of the parenchyma, collapse of the alveoli and marked polymorphonuclear infiltration of all sections, with much débris, blood pigment and red cells. Arteries and veins accompanied the bronchi, and the pleural vessels were markedly dilated. The pleura was covered with fibrin. The bronchi were not remarkable. The parenchyma showed some disintegrating lung tissue and some with an acidophilic, granular appearance. The nuclei were pyknotic and were disintegrating in many areas.

The left lung showed some areas of atelectasis but no inflammatory infiltration, and there was no emphysema.

EMBRYOLOGY AND PATHOGENESIS

The most tenable embryologic explanation for this condition is the failure of development of the right sixth aortic arch. The right pulmonary artery, embryologically, is an outgrowth from the right sixth aortic arch and is given off about halfway between the dorsal and the ventral aorta (Bremer [3]). The left sixth aortic arch gives rise to the left pulmonary artery and the ductus arteriosis; in this case it developed normally, since those structures were present and normal.

The bronchial arteries, originating in the thoracic aorta or in the intercostal arteries and following the bronchi into the lung, were probably sufficient to maintain the circulation of the lung in the prenatal atelectatic condition, the pulmonary arteries normally being quite small and not having much function in fetal life. When the function of the lungs was established at birth, however, the sudden need for more blood could not be met by the bronchial vessels alone, and the result was ischemia of the right lung, which resulted in necrosis in the following four days. On the fourth day rupture occurred and pneumothorax resulted.

The question that arises, however, is whether absence of a pulmonary artery alone produces sufficient ischemia to result in necrosis without other complicating circumstances. Horine and Warner,[4] Schlaepfer,[5] and Smirnoff [6] tied off the pulmonary arteries in animals, and no marked necrosis took place, the only result being hyperemia and desquamation of alveolar lining cells, with subsequent fibrosis. The collateral bronchial circulation apparently was adequate to prevent necrosis. Schlaepfer [5] reported three cases in which the pulmonary artery had been ligated for abscess of the lung without gangrene's taking place. He reported improvement of the patients. Smirnoff [6] stated that to produce gan-

3. Bremer: Am. J. Anat. **1**:137-144, 1902.

4. Horine, C. F., and Warner, C. G.: Experimental Occlusion of the Pulmonary Artery, Arch. Surg. **28**:139-149 and 150-159 (Jan.) 1934.

5. Schlaepfer, Karl: Ligation of the Pulmonary Artery of One Lung With and Without Resection of the Phrenic Nerve, Arch. Surg. **9**:25-94 (July) 1924; Am. Rev. Tuberc. **10**:35-66, 1924.

6. Smirnoff, S. A.: Ann. Surg. **84**:317-322 (Sept.) 1926.

grene both the pulmonary and the bronchial arteries, or the bronchial vessels and the pulmonary veins must be tied off. It must be remembered, however, that these findings are on adult organisms. The more rapid cellular metabolism and the increased production of lactic acid in the tissues of the new-born render their tissues more susceptible than those of adults to lack of blood supply (György [7]). The metabolism of this rapidly growing tissue approaches that of tumor tissue, of which the tendency to necrosis when an inadequate blood supply is being received is well recognized.

The polymorphonuclear reaction and fever were probably reactions to toxic absorption from necrotic tissue. No convincing clinical evidence of infection was present. The total absence of cellular reaction in the left lung discredits the possibility that infection was an important factor in the production of pathologic changes, although infection was probably secondarily present in the right lung at death.

SUMMARY

The case of a new-born infant with congenital absence of the right pulmonary artery, gangrene of the right lung, secondary rupture of the lung and pneumothorax is reported, and postmortem observations are presented.

The embryology of the lesion, the probable pathogenesis and the sequence of events are discussed.

The reported case is apparently unique in the recent medical literature, and absence of the pulmonary artery constitutes a new cause of spontaneous pneumothorax in the new-born.

64½ North Second Street.

7. György, P.: Growth, Structure, Metabolism and Nutrition of the Healthy Infant, in von Pfaundler, M., and Schlossmann, A.: The Diseases of Children, translated by M. G. Peterman, Philadelphia, J. B. Lippincott Company, 1935, vol. 1, p. 243.

CYCLIC VOMITING OF OCULAR ORIGIN

JEROME GLASER, M.D.
AND
MACY L. LERNER, M.D., M.Sc. (OPH.)
ROCHESTER, N. Y.

For the purposes of this discussion we consider the term cyclic vomiting synonymous with the terms periodic vomiting, recurrent vomiting and acetonemic vomiting, the last term being preferred by French pediatricians. The condition begins in early childhood and usually terminates with puberty or earlier. It is characterized by repeated attacks of vomiting which occur at regular or irregular intervals of a few weeks or a few months and are sometimes accompanied by fever, headache and abdominal pain. According to Marfan,[1] it was first described by Gruère, in 1840. The attacks are resistant to any form of treatment but usually disappear spontaneously in the course of several days. A few cases in which the outcome was fatal have been reported, with negative observations at necropsy.

The consensus among pediatricians, with whom we are in complete agreement, is that cyclic vomiting is not a specific disease entity but is a symptom complex which may result from a variety of causes, among which may be mentioned infections, especially acute infection of the upper part of the respiratory tract, tonsillitis, chronic appendicitis and syphilis; metabolic conditions, such as allergy, faulty fat metabolism, spontaneous hypoglycemia, adrenal insufficiency, ketosis and fatigue; gastro-intestinal conditions, especially intermittent high obstructions, gastro-enteroptosis and constipation, and orthopedic conditions, such as faulty posture which results in gastro-enteroptosis. In all complete discussions of the subject, with the notable exception of the otherwise complete discussion by Marfan,[1] eye strain is mentioned as a possible etiologic factor. We have, however, been able to find in the literature specific mention of only two cases.

Le Wald[2] in 1926 reported the case of a girl 15 years of age who had had attacks since the age of 12 years at irregular intervals

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From the Departments of Pediatrics and Ophthalmology of the University of Rochester School of Medicine and Dentistry.

1. Marfan, A. B.: Les vomissements périodiques avec acétonémie, Paris, Masson & Cie, 1926.

2. Le Wald, L. T.: "Cyclic Vomiting" in Infants and Children, Radiology 7:410 (Nov.) 1926.

of from one to three months. She also had strabismus. All efforts to relieve the cyclic vomiting were unavailing until the strabismus was corrected surgically. After that the vomiting did not recur.

Sherman and Koenig [3] in 1930 in a report based on fifty cases collected over a period of eighteen years made the statement, not borne out in our practice, that eye strain is rare in young children. One of their patients, a boy, had on numerous occasions the customary prodromal signs and symptoms of a commencing attack. They were always promptly relieved by the adjustment of his glasses.

The occurrence of five cases of cyclic vomiting in our practice in which the condition was unrelieved until refractive errors were corrected seems worthy of reporting.

CASE 1.—The patient, a girl, had been under the care of one of us since birth. At the age of 2 years typical attacks of cyclic vomiting of the textbook variety just described developed. The family history revealed no pertinent condition except allergy. The attacks were treated symptomatically without success. During one severe attack a sufficient amount of a mixture of the hydrochlorides of the opium alkaloids was given by hypodermic injection to put the child in a state of narcosis, and during the whole of that night the child, even though apparently unconscious, had mild attacks of vomiting regularly every half-hour. Examination gave no clue as to the cause of the condition. Elimination diets were tried without success. Although there were no symptoms of ocular trouble, because of the knowledge that the disease might in apparently rare instances have an ocular basis, refraction was performed after the use of atropine when the child was 3 years old. The essential finding was spherical hyperopia of 2.5 diopters. The child wore the prescribed correction without difficulty, and the attacks of vomiting disappeared, to reappear only on occasions when she did not wear the glasses for one reason or another. The attacks which then recurred could be easily checked by replacing the glasses. At the age of 6 years the child was, however, able to discard the glasses for long periods without recurrence of the vomiting.

CASE 2.—In the patient, a boy who had been under the care of one of us since birth, attacks of vomiting developed at the age of 18 months, after what was probably atypical whooping cough of about five weeks' duration. At first the attacks were thought to be incidental to the infection, but as time went on they became recognizable as typical attacks of cyclic vomiting. They were unrelieved by the usual measures, and soluble phenobarbital U. S. P. (sodium phenobarbital) and sodium amytal administered rectally seemed to cause a type of maniacal excitement rather than to give rest and relief from the vomiting. Complete examination and allergic studies, including cutaneous tests, gave no clue to the cause of the condition. When 2 years old the child, who had attacks every four to six weeks, began complaining of pain in his eyes. This is rather difficult to believe, but the mother states that the pain was indicated by frequent rubbing of the eyes, with repetition of the word hurt. Despite our success in the previous case, we were rather skeptical of the value of refraction for this condition in one so young. Nevertheless, the child was examined after the use of atropine at the age of 25 months. The essential

3. Sherman, W. H., and Koenig, E. C.: Concerning Causes of Cyclic or Recurring Vomiting in Children and the Prevention of the Attacks, Acta pædiat. **11**:392, 1930.

findings were spherical hyperopia of 2½ diopters and ¾ diopter of hyperopic astigmatism. The child wore the correction with delight. He had one attack of vomiting six months later, during an acute infection of the upper part of the respiratory tract of a type rather prevalent at that time and accompanied characteristically by vomiting. At the age of 4 years he had had no subsequent attacks.

CASE 3.—The patient was a girl 6 years of age who had had frequent attacks of vomiting of a cyclic nature since early infancy. The slightest excitement brought on an attack. Riding in an automobile or a train aggravated the condition. She had been studied by various physicians, including pediatricians, without obtaining relief. At the age of 7 years her condition was such that a slowly growing tumor of the brain was suspected, and she was seen in consultation for the purpose of examining the eyegrounds. At that time a markedly oval disk, suggesting astigmatism, was noted, and since there was no papilledema or other abnormality of the fundus it was decided that refraction should be performed. This was done after the use of atropine. The findings were 2 diopters of spherical hyperopia and 3 diopters of hyperopic astigmatism in each eye, axis 90. The visual acuity was only 6/60 without correction. Glasses produced almost miraculous relief. During the following year the child vomited only twice, and in the seven years following the refraction she vomited only once more.

CASE 4.—The patient was a boy who had had attacks of cyclic vomiting at two or three week intervals since the age of 2 years. The attacks lasted for from three to four days and were characterized by extreme dehydration, since fluids could be retained only after parenteral administration. The child was known to be allergic, and it was suspected that he was sensitive to various foods, but elimination of these from the diet gave no relief. When he was 7 years old refraction was performed after the use of atropine, with the finding of 1 diopter of astigmatism of the mixed type. Wearing glasses gave marked relief, which in the course of a year or two became permanent.

CASE 5.—The patient was an infant 2½ years of age who was referred to us because since early infancy she had had a marked tendency to turn her head to one side in fixing her gaze. There was also a history of frequent vomiting of a cyclic character, which had not responded to the usual therapeutic measures. It was noted that the child also tilted her head to the left, suggesting so-called ocular torticollis. Examination after the use of atropine revealed compound hyperopic astigmatism of 2½ diopters. When the child wore the refraction the torticollis slowly improved and the vomiting, at first greatly relieved, gradually completely disappeared. The child was under observation for two years and was free from vomiting for the second year.

These case reports indicate that the symptom complex of cyclic vomiting may have an ocular basis much more frequently than is generally suspected. Our experience leads us to believe that in cases of cyclic vomiting the cause of which is not discovered with the usual methods of study refraction should be performed after the use of atropine regardless of the age of the patient.

ALLERGIC TUBERCULOUS PURPURA

H. P. WRIGHT, M.D.
AND
H. L. BACAL, M.D.
MONTREAL, CANADA

It has been known for a long time that purpura occurs in the last stages of tuberculosis, and "one of the earliest references to a possible association between these two conditions is found in Willan's Treatise on Cutaneous Diseases (1801). He says 'Purple spots occur in the last stage of pulmonary consumption as the immediate forerunners of death.'" [1] Cruice [2] in 1912 said that in the last 1,000 cases at the Adirondack Cottage Sanitarium Brown had only three with purpura and that among 1,626 cases of tuberculosis in the wards at the Henry Phipps Institute of the University of Pennsylvania in Philadelphia only eight instances of purpura were observed.

However, it should be remembered that purpura is more likely to occur in cases of miliary and generalized tuberculosis, that this class of case is rare in sanatoriums and that therefore the statistics just cited may be misleading.

Occasionally purpura in children in the last stages of miliary tuberculosis has been observed in Montreal. During the last fifteen years in Montreal, as far as can be ascertained, in no case except the one to be reported here did purpura occur coincidentally with a marked tuberculin reaction, and reference to the literature has not brought to light any case in a human being of purpura resulting from the intracutaneous injection of old tuberculin, although Baize [3] reported two instances of purpura in tuberculosis, one in an infant 9 months of age and the other in a child 8 years old. Both had positive reactions to tuberculin, and in the infant the area of the reaction was purpuric in the center. Both patients recovered.

Read before a joint meeting of the American Pediatric Society and the Canadian Society for the Study of Diseases of Children, Bolton Landing, N. Y., June 11, 1936.

From the Department of Paediatrics, McGill University Faculty of Medicine, and the Children's Memorial Hospital.

1. Jones, Harold W., and Tocantins, L. M.: M. Clin. North America **16**:181, 1932.

2. Cruice, J. M.: Am. J. M. Sc. **144**:875, 1912.

3. Baize, P.: Monde méd., Paris **43**:914, 1933.

In 1931 Greengard,[4] of the Cook County Children's Hospital, reviewed the literature and reported two cases of purpura, one in a child 3 years of age who died of miliary tuberculosis and the other in a girl 11 years of age whom he considered to present a typical example of cachectic purpura occurring in chronic tuberculosis. The girl died four months after admission to the hospital. Greengard considered that both patients exhibited one definite factor—evidence of capillary damage demonstrable by the Hess test. Also both patients were anergic and failed to respond to the intracutaneous injection of old tuberculin (the amount injected was not stated).

Jones and Tocantins [1] stated:

> In order to have a clear conception of purpura, it is necessary to minimize the importance of platelet deficiency and to emphasize that of capillary hyperpermeability as an etiologic factor, and to recognize that multiple factors enter into the question of permeability of the capillaries and accordingly in the production of the disease. . . .
>
> Duke reported several cases of purpura in association with tuberculosis and attempted to produce the condition experimentally by injection of tuberculin into rabbits. In a few of the animals he produced a marked reduction of platelets, but was unable to produce the symptom complex of purpura. Peterson, however, showed that in a tuberculous animal the capillaries are altered, and by numerous experiments demonstrated that in this disease they are at times highly permeable.

REPORT OF A CASE

R. B., a white boy aged 13 years, with three other children of the family, came to the outpatient department of the Children's Memorial Hospital on May 7, 1934, for routine examination because his father had recently died of tuberculosis and diabetes, a brother had a tuberculous knee and was in a hospital, and a sister had tuberculosis.

The physical examination showed the boy to be apparently healthy except for several carious teeth and cervical adenopathy. The Mantoux test was made with 0.1 cc. of a 1:1,000 solution of old tuberculin (0.1 mg.) on the flexor surface of the right forearm, and it was requested that a roentgenogram of the chest be made if the tuberculin test gave a positive reaction. The patient was referred also to the dental clinic. On May 8 two carious teeth were easily extracted under local anesthesia, 2 per cent procaine hydrochloride being used. On May 9 the area of the tuberculin test showed a markedly positive reaction, measuring 20 by 45 mm., with a small necrotic area (++++). The roentgenogram of the child's chest showed that his heart was slightly larger than average. The aorta, the trachea and the domes of the diaphragm were normal. There was a slight increase in the right root shadow, and bronchial markings were accentuated to the base of the right lung. No calcification was seen, and there was no evidence of active tuberculosis in the parenchyma of the lung.

The Mantoux test was made on the three other children at the same time, using the same solution of old tuberculin and the same dose. Two of the children tested showed moderately positive reactions (++) to the intracutaneous injections.

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4. Greengard, J.: Am. Rev. Tuberc. **24**:452, 1931.

The patient was not seen again until May 14, when he returned to the outpatient department. His mother stated that on May 10 a rash had developed around the area of the tuberculin test on his forearm. This rash had spread gradually, and by May 13 it was present on all of the child's extremities and on his trunk. Up to that time there were no symptoms associated with the rash, except perhaps some irregular fever.

The boy was admitted to the hospital. The rectal temperature was 100 F. and rose gradually, by the next day reaching 102 F. The pulse rate also increased,

TABLE 1.—*Observations on Blood Smear*

Date	Number of White Cells	Percentages								Stippled Red Cells	Polymorphonuclear Leukocytes, Types According to Arneth Index				
		Polymorphonuclear Neutrophils	Lymphocytes	Monocytes	Eosinophils	Basophils	Metamyelocytes	Blasts	Basket Cells		I	II	III	IV	V
5/15/34	3,550	56	7	15	12	1	..	..	9	.....	56	34	10		
5/16/34	2,350	35	25	19	14	1	..	..	6	.....					
5/17/34	2,400	29	21	15	29	2	..	..	4	.....	60	30	8	2	
5/18/34	1,500	28	39	13	12	..	..	1	7	.....					
5/19/34	6,250	53	20	10	9	1	2	1	4	.....					
5/21/34	4,850	53	17	13	6	1	..	..	10	.....					
5/19/34	6,250	53	20	10	9	1	2	1	4	.....					
5/23/34	6,700	52	25	13	2	2	..	..	6	.....	14	46	32	8	
5/25/34	6,250	65	18	10	1	2	..	..	4	Several					
5/26/34	6,750	46	24	15	1	3	2	..	9	Numerous					
5/28/34	6,350	42	28	15	2	3	1	..	9	Many					
6/ 5/34	7,400	56	27	13	2	2	..	..	..	Few					
6/ 7/34	7,400	45	36	15	1	..	..	..	3	Marked					
6/ 9/34	8,600	65	21	11	1	1	1	..	..	Few					

TABLE 2.—*Atopens Used in Allergic Tests*

1. Cat hair	14. Cattle dander	27. Ragweed (giant)	39. Cottonseed
2. Milk	15. Dog hair	28. Pyrethrum	40. Corn
3. Orris root	16. Goldenrod	29. June grass	41. Onion
4. Beet	17. Wheat	30. Duck feathers	42. Rice
5. Silk	18. Horse dander	31. Kapok	43. Cabbage
6. Egg	19. Oat	32. Chicken	44. American cheese
7. Goose feathers	20. Rabbit hair	33. Strawberry	45. Tobacco
8. Lamb	21. Orange	34. Beet	46. Banana
9. Rye	22. Timothy	35. Dust	47. Cocoa
10. Dried apple	23. Chicken feathers	36. Herring	48. Pea
11. Red top	24. Sheep wool	37. Potato	49. Bean
12. Veal	25. Ragweed (short)	38. Haddock	50. Codfish
13. Orchard grass	26. Tomato		

None of these elicited a positive reaction.

from 90 to 120 per minute. The heart and the lungs appeared clinically to be normal, and the spleen was barely palpable below the costal margin. The blood pressure was 130 systolic and 78 diastolic. Several carious teeth still were present. The fundi seemed normal.

The skin showed a widespread maculopapular eruption on the extremities, particularly the flexor surfaces of the arms (fig. 1), thighs and legs. Scattered lesions were present on the trunk and the buttocks and in the mucous membrane of the mouth. The lesions were cyanotic and petechial and did not disappear on pressure.

On May 15, six days after the first roentgenogram of the chest had been made, a second roentgenogram showed that the heart shadow had markedly decreased and that there was no demonstrable change in the lungs.

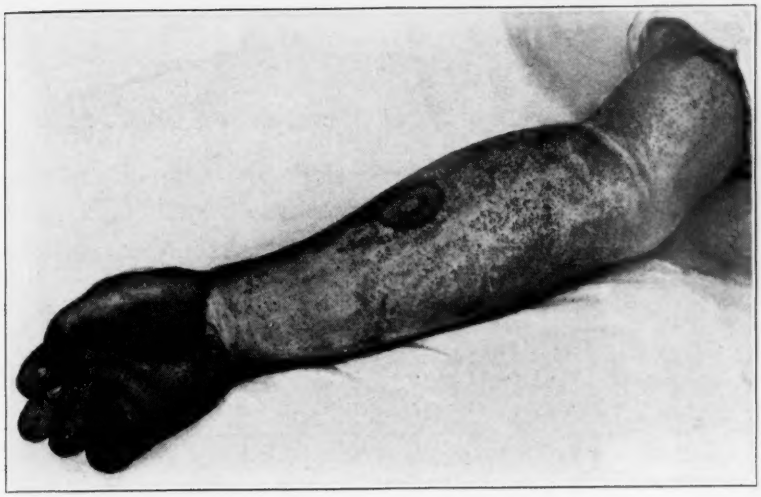

Fig. 1.—Allergic tuberculous purpura (May 14, 1934). The Mantoux test had been made on May 7, 1934, with 0.1 cc. of a 1:1,000 solution of old tuberculin (0.1 mg.).

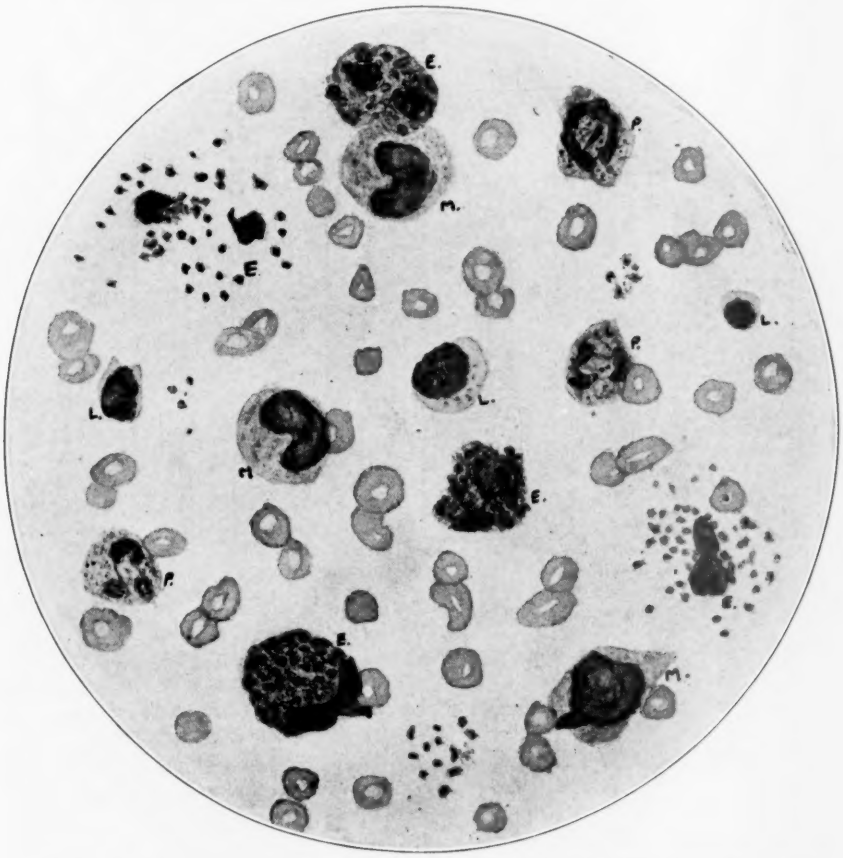

Fig. 2.—Composite picture of the blood (May 17, 1934). The hemoglobin content was 82 per cent (Hellige). The red cells numbered 4,800,000, the platelets 170,000 and the white cells 2,400, with 29 per cent polymorphonuclear neutrophils (marked *P.*), 21 per cent lymphocytes (marked *L.*), 15 per cent monocytes (marked *M.*), 29 per cent eosinophils (marked *E.*), 2 per cent basophils and 4 per cent basket cells.

Table 1 demonstrates the leukopenia, eosinophilia, shift to the left and stippling. On June 5 roentgenograms of the right knee and the wrist showed no evidence of increased density (no lead line).

A composite picture of the blood on May 17, 1934 (fig. 2), was prepared by Miss E. H. Gray. The clotting time was three and one-half minutes, and the clot retraction was normal. The bleeding time was two and one-fourth minutes. The Hess test was not made. The rate of sedimentation was 11.

Fig. 3 shows the correlation of the temperature and the number of leukocytes and of eosinophils.

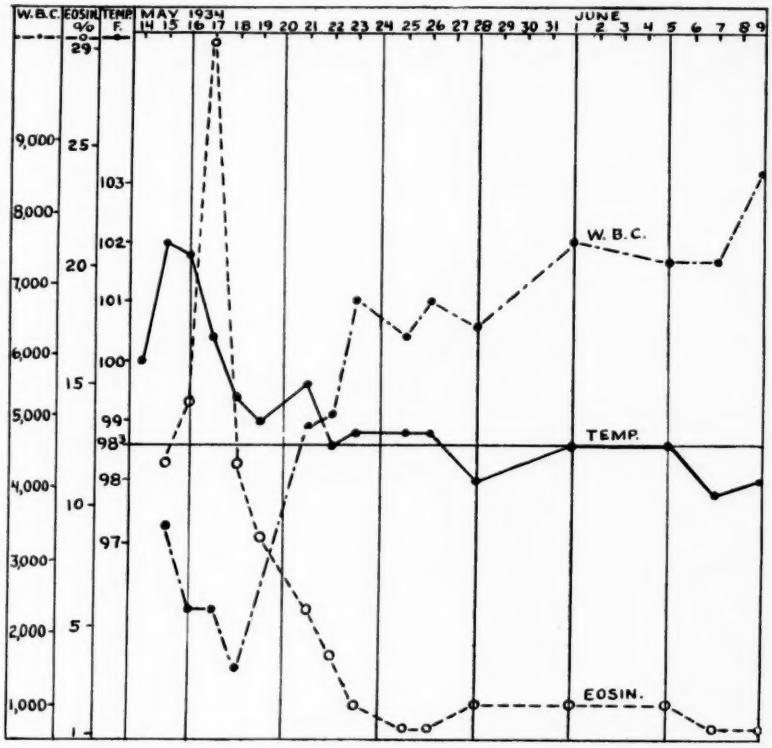

Fig. 3.—Correlation of the temperature and the number of white cells and of eosinophils.

Patch tests were made with phenol and procaine hydrochloride and gave negative results. The diluted tuberculin contained 0.25 per cent phenol in physiologic solution of sodium chloride, and procaine hydrochloride had been used in extracting the carious teeth.

Table 2 lists the fifty commoner atopens which were used in cutaneous tests to determine sensitivity to protein on May 22. All gave negative results. A Wassermann test of the blood gave a negative result. The urine was normal. Uric acid in the blood measured 2.43 mg. per hundred cubic centimeters, and the calcium content of the blood was 10.4 mg. per hundred cubic centimeters.

One week after the patient's admission to the hospital, the fever had subsided, the spleen was no longer palpable and the purpura had disappeared. Tuberculin

tests with varying dilutions were then made, the strength being gradually increased until the same amount of old tuberculin was injected as had apparently caused the first attack of purpura. Table 3 indicates the procedure and shows the results.

There was no recurrence of the purpuric lesions. Presumably the patient had become partially desensitized to tuberculin.

On June 15 he was discharged in good condition, with no purpura but with fading reactions to tuberculin. From that date to May 30, 1935, he was well and gained 15 pounds (6.8 Kg.), but on that date he was readmitted for investigation.

TABLE 3.—*Tuberculin Tests with Various Dilutions at Varying Intervals*

Date	Strength	Result
5/26/34	1. 1:100,000	Negative
5/30/34	2. 1: 10,000	Positive: 20 by 15 mm. area of tuberculin test made 5/26 showing as area of erythema size of pea
6/ 8/34	3. 1: 1,000	Positive: Area of edema, 50 by 50 mm., and of erythema, 65 by 65 mm.; no lymphangitis

At no time was there any recurrence of the purpuric lesions following the tuberculin or other tests.

TABLE 4.—*Tuberculin Test Made with 1: 100 Solution (1 mg.) on Left Forearm*

Date	Time	Results
5/30/35	5:30 p.m.	Temperature (rectal), 99.4 F.
	7:30 p.m.	Swelling and redness 1 inch in diameter; temperature, 100 F.
5/31/35	9:30 a.m.	Systemic reaction with headache; temperature, 101.4 F.; reaction to old tuberculin very positive, 2 by 3 inches, with streak of lymphangitis 5 inches long; left axillary gland enlarged and tender; reddish mottled area in right forearm (test of 1934)
	5:00 p.m.	Positive reaction same size; temperature, 100 F.; lymphangitis 6 inches long; petechial hemorrhages at site of injection
6/ 1/35	9:00 a.m.	Fine petechiae on right forearm; temperature, 99 F.
	5:00 p.m.	Fading of reaction but petechiae present on both arms; temperature, 99 F.
6/2-4/35		No reaction on right forearm; few petechiae on left forearm; Hess test above left forearm, producing numerous petechial hemorrhages, particularly over area of reaction
6/ 7/35		Discharged; general condition good; peeling over area of tuberculin test

The examination gave essentially negative results except for showing several carious teeth. A roentgenogram of the lungs showed no significant change from the condition revealed in that taken a year previously. The boy was discharged from the hospital in good condition on June 7.

Table 4 demonstrates the resultant purpura following the intradermal injection of 1 mg. of old tuberculin.

COMMENT

This case is reported because of the extreme rarity of the occurrence of proved allergic tuberculous purpura.

Progress in Pediatrics

GRADED SEQUENCE IN POSTURAL AND IN LOCOMOTOR DEVELOPMENT

ITS RELATIONSHIP TO THE MATURATION OF THE CENTRAL NERVOUS SYSTEM

HAROLD ABRAMSON, M.D.
NEW YORK

Since there cannot be a function without a structure nor a structure without a function, development implies concomitant changes in structure.[1]

One of the important problems in medicine and psychology today is that of genesis of human behavior. Within recent years heightened interest has given considerable impetus to the study of the subject, and with the elaboration of more adequate methods of approach a better understanding of the fundamental nature of behavior is gradually evolving. Activity has been particularly great in the field of child psychology, much progress having been made between the pioneer efforts of Comenius (1592-1670) [2] and the present day organized applications of the principles of experimental science [3] to investigations on the behavior of infants and young children.

It is not within the scope of this paper to review historically the extensive literature on the subject. Reference may be had to the critical survey by Murphy [4] and to the summary by Coghill [5] of the more important researches in the fields of animal and human behavior. Dewey [6] recently published an excellent review of the literature during

From the department of pediatrics of the Beth Israel Hospital, service of Dr. Herman Schwarz.

1. Frank, L. K.: The Problem of Child Development, Child Development **6**:7-18 (March) 1935.

2. Rusk, R. E.: A History of Infant Education, London, University of London Press, 1933, pp. 11-18.

3. Cohen, M. R.: The Ideals of Science, in Reason and Nature, New York, Harcourt, Brace and Company, Inc., 1931, pp. 83-114.

4. Murphy, G.: An Historical Introduction to Modern Psychology, New York, Harcourt, Brace and Company, Inc., 1929, pp. 279-288.

5. Coghill, G. E.: The Neuro-Embryologic Study of Behavior: Principles, Perspective and Aim, Science **78**:131-138 (Aug. 18) 1933.

6. Dewey, Evelyn: Behavior Development in Infants: A Survey of the Literature on Prenatal and Postnatal Activity, 1920-1934, New York, Columbia University Press, 1935.

the years of 1920 to 1934 on the prenatal and postnatal behavioral development of the human fetus and infant. However, it should be stated that much of the present knowledge on the genesis of behavior has been derived from experimental studies on lower and higher forms of animal life. The general trend of these investigations has been toward establishing the interrelationship of the development of behavior and the maturation of the nervous system to explain adjustive reactions adequately in terms of cerebral structure. The researches of Tracy,[7] Avery,[8] Coghill,[9] Langworthy,[10] Tilney and Kubie,[11] Kuo,[12] Tilney,[13] Corionos,[14] Carmichael,[15] and others [16] serve to reaffirm the close connection between the ripening of the nervous system and the development of somatic behavior in animals. Comparatively few neuro-

7. Tracy, H. C.: Development of Motility and Behavior Reactions in Toadfish (Opsanus Tau), J. Comp. Neurol. **40**:253-369 (April) 1926.

8. Avery, G. T.: Responses of Foetal Guinea Pigs Prematurely Delivered, Genetic Psychology Monographs, Worcester, Mass., Clark University Press, 1928, vol. 3, no. 4, pp. 252-331.

9. Coghill, G. E.: Anatomy and the Problem of Behavior, London, Cambridge University Press, 1929.

10. Langworthy, O. R.: Behavior in Pouch-Young Opossums Correlated with Myelinization of Tracts in Nervous System, J. Comp. Neurol. **46**:201-247 (Aug.) 1928; A Correlated Study of the Development of Reflex Activity in Fetal and Young Kittens and the Myelinization of Tracts in the Nervous System, Contrib. Embryol. (nos. 109-117) **20**:127-171 (Jan.) 1929.

11. Tilney, F., and Kubie, L. S.: Behavior in Its Relation to the Development of the Brain, Bull. Neurol. Inst. New York **1**:229-213 (June) 1931.

12. Kuo, Z. Y.: Ontogeny of Behavior in Aves: I. The Chronology and General Nature of the Behavior of the Chick Embryo, J. Exper. Zoöl. **61**:395-430 (April 5) 1932.

13. Tilney, F.: Behavior in Its Relation to the Development of the Brain: II. Correlation Between Development of Brain and Behavior in Albino Rat from Embryonic States to Maturity, Bull. Neurol. Inst. New York **3**:252-358 (June) 1933.

14. Corionos, J. D.: Development of Behavior in the Fetal Cat, Genetic Psychology Monographs, Worcester, Mass., Clark University Press, 1933, vol. 14, no. 4, pp. 283-386.

15. Carmichael, L.: An Experimental Study in the Prenatal Guinea Pig of the Origin and Development of Reflexes and Patterns of Behavior in Relation to the Stimulation of Specific Receptor Areas During the Period of Active Fetal Life, Genetic Psychology Monographs, Worcester, Mass., Clark University Press, 1934, vol. 16, nos. 5 and 6, pp. 337-491.

16. Orr, D. W., and Windle, W. F.: The Development of Behavior in Chick Embryos: The Appearance of Early Somatic Movements, J. Comp. Neurol. **60**: 271-288 (Oct.) 1934. Windle, W. F., and Orr, D. W.: The Development of Behavior in Chick Embryos: Spinal Cord Structure Correlated with Early Somatic Motility, ibid. **60**:287-307 (Oct.) 1934. Loo, Y. T.: Postnatal Myelogenesis of the Cerebral Cortex, National Research Institute of Psychology, Shanghai, Academia Sinica, June 1933, vol. 1, pp. 1-13.

physiologic studies [17] have been carried out on the human fetus and infant, the difficulties involved being obvious. However, experimental observations in this field also suggest that the orderly development of somatic behavior patterns in the human being is dependent on the unaltered growth of specific neural counterparts in the nervous system.

THE GRADED MOTOR SEQUENCE

Of the systems of human behavior, that relating to motor activity lends itself perhaps most readily in all its successive phases of unfolding to present day objective methods of clinical and neurophysiologic investigation. In the development of the human infant, most outstanding and certain in its general course is the progressive unfolding of postural and locomotor traits from the time the infant is in the early fetal position until he moves in the erect posture. In particular, the

17. Erbkam: Lebhafte Bewegung eines viermonatlichen Fötus, Neue Ztschr. f. Geburtsk. **5**:324-326, 1837. Zuntz, N.: Ueber dis Respiration des Säugethier-Foetus, Arch. f. d. ges. Physiol. **14**:605-627, 1877. Pflüger, E.: Die Lebensfähigkeit des menschlichen Foetus, ibid. **14**:628-629, 1877. Preyer, W.: Die Bewegungen des menschlichen Foetus, in Specielle Physiologie des Embryo, Leipzig, T. Grieben, 1885, pp. 429-440. Mermann: Ueber eigenthümliche rhythmische Fötalbewegungen, Centralbl. f. Gynäk. **11**:622-624 (Sept. 24) 1887. Ikeda, J.: Ueber anfallsweise auftretende rhythmische Fötalbewegungen und Hernia diaphragmatica congenita, ibid. **17**:1089-1091 (Nov. 25) 1893. Lui, A.: Quelques observations sur le développement histologique de l'écorce cérébelleuse par rapport à la faculté de se tenir debout et de marcher, Arch. ital. de biol. **21**:395-397, 1894. Strassman, P.: Das Leben vor der Geburt, Samml. klin. Vortr. no. 353, 1903 (Gynäk. no. 132, pp. 947-967). Ahlfeld, F.: Die intrauterine Tätigkeit der Thorax- und Zwerchfellmuskulatur, intrauterine Atmung, Monatschr. f. Geburtsh. u. Gynäk. **21**:143-163, 1905. Bumm, E.: Grundriss zum Studium der Geburtshülfe, Wiesbaden, J. F. Bergmann, 1907, pp. 75-88. Yanase, J.: Beiträge zur Physiologie der peristaltischen Bewegungen des embryonalen Darmes, Arch. f. Physiol. **117**:345-383, 1907; **119**:451-564, 1907. Krabbe, K.: Les réflexes chez le foetus, Rev. neurol. **24**:434-435, 1912. Winterstein, H.: Ueber Leben eines menschlichen Fötus bei künstlicher Durchspülung, Zentralbl. f. Physiol. **28**:728, 1914. Sarwey, O., in Döderlein, A.: Handbuch der Geburtshülfe, Wiesbaden, J. F. Bergmann, 1915, pp. 180-213. Minkowski, M.: Réflexes et mouvements de la tête, du tronc et des extrémités du foetus humain pendant la première moitié de la grossesse, Compt. rend. Soc. de biol. **83**:1202-1204 1920. Bersot, H.: Développement réactionnel et réflexe plantaire du bébé né avant terme à celui de deux ans, Schweiz. Arch. f. Neurol. u. Psychiat. **7**:212-239, 1920; **8**:47-74, 1921. Bolaffio, M., and Artom, G.: Richerche sulla fisiologia del sistema nervoso del feto umano, Arch. di sc. biol. **5**:457-487 (June) 1923-1924. Minkowski, M.: Neurobiologische Studien am menschlichen Foetus, in Abderhalden, E.: Handbuch der biologischen Arbeitsmethoden, Berlin, Urban & Schwarzenberg, 1928, vol. 5, pt. 5B, no. 4, pp. 511-618. de Crinis, M.: Die Entwicklung der Grosshirnrinde nach der Geburt in ihren Beziehungen zur intellektuellen Ausreifung des Kindes, Wien. klin. Wchnschr. **45**:1161-1165 (Sept. 23) 1932. See Dewey [6] for additional literature between the years 1920-1934.

first two years of life are characterized by the rapid appearance of the fundamentals of motor skills. Likewise, they are a period of rapid physical growth. There is nothing irregular or haphazard in the development of motor phenomena; nor are the continuous series of developmental events dependent on chance. On the contrary, the growth of motor activities displays a logical sequence, its course being governed apparently by biologic laws strikingly similar to those controlling the logical course of physical growth.

In the description of the successive phases of motor development, no attempt will be made to enter into a detailed exposition of the numerous behavioral items contributing toward its total growth pattern. For such exposition reference may be had to the analytic studies by Gesell and his co-workers,[18] Shirley,[19] Bühler,[20] Jones [21] and other students in this field.[22] Only the more important stages in postural and locomotor development will be discussed, in outline form and from a broad point of view. It should be borne in mind that at all times the organism reacts in a unitary manner, the various parts of the body making adjustments in relation to one another so that development of each phase of activity in one portion of the body is accompanied by secondary phenomena in other parts. Mention should also be made of the factor of age in its relation to motor development. Gesell [23] stressed the fact that "development is a function of age, and that a recognition of the age values of behavior and of the behavior values of age constitutes the first essential for developmental diagnosis."

Just as in physical growth development spreads downward from the cephalic end of the organism in a caudal direction, a phenomenon which will be discussed subsequently, similarly in motor development control

18. Gesell, A.: Infancy and Human Growth, New York, The Macmillan Company, 1929; An Atlas of Infant Behavior, New Haven, Conn., Yale University Press, 1934, vol. 1. Gesell, A.; Thompson, H., and Amatruda, C. S.: Infant Behavior: Its Genesis and Growth, New York, McGraw-Hill Book Company, 1934, pp. 48 and 97.

19. Shirley, M. M.: The First Two Years: Postural and Locomotor Development, Minneapolis, University of Minnesota Press, 1931, vol. 1.

20. Bühler, C.: The First Year of Life, New York, The John Day Company, 1930.

21. Jones, M. C.: The Development of Early Behavior Patterns in Young Children, Pedagog. Semin. & J. Genetic Psychol. **33**:537-585 (Dec.) 1926.

22. Blanton, M. G.: The Behavior of the Human Infant During the First Thirty Days of Life, Psychol. Rev. **24**:456-483 (Nov.) 1917. Oseretzky, N. I.: Eine metrische Stufenleiter zur Untersuchung der motorischen Begabung bei Kindern, Ztschr. f. Kinderforsch. **30**:300-314 (June 25) 1925. Cunningham, B. V.: An Experiment in Measuring Gross Motor Development of Infants and Young Children, J. Educ. Psychol. **18**:458-464 (Oct.) 1927.

23. Gesell, A.: Infant Behavior in Relation to Pediatrics, Am. J. Dis. Child. **37**:1055-1075 (May) 1929.

migrates down over the body from head to tail. The unfolding of coordinated movements begins in the area of the head, spreading down through the neck and the trunk to the tail region, with a concomitant spread of activity from the shoulders out to the fingertips and from the hips out to the toes. In this connection, Dewey [24] called attention to the confusing inaccuracy that frequently appears in the literature on human behavior due to the assumption that development of the lower limbs occurs in a continuum after control of the caudal region is established and to the failure of writers to give the term cephalocaudal its proper meaning, head to tail, not head to feet.

The motor equipment of the new-born infant, aside from a few highly specialized reflex responses,[25] consists essentially of diffuse mass activities seemingly aimless in character. These random movements or total bodily reactions [26] are, however, of great importance in that they form the basis of all subsequent motor responses of the infant. Observation [27] of the new-born infant in the prone position will reveal the typical posture of general bodily flexion; the weight of the body rests on the face, chest, stomach and knees (fig. 1). General somatic activity consists of occasional side to side movements of the head and feeble random movements of the arms and legs, the latter soon giving way to uncontrolled twisting, stretching and squirming movements and increased motion of the head from side to side. The first evidence of development is seen in the area of the head, when the infant lifts his head and chin off the table. The wave of development then spreads down to the shoulders and trunk, and the infant is able to raise his chest off the table top, his weight being supported on the forearms and elbows. The back assumes an attitude of extreme extension, the head is held high and there is better coordination of the head-turning move-

24. Dewey,[6] pp. 298 and 299.

25. Burr, C. W.: The Reflexes in Early Infancy, Am. J. Dis. Child. **21**:529-533 (June) 1921. de Angelis, F.: Reflexes of the New-Born, ibid. **26**:211-215 (Sept.) 1923. Magnus, R.: Animal Posture, Proc. Roy. Soc., London, s.B **98**: 339-353 (Aug. 1) 1925. Schaltenbrand, G.: The Development of Human Motility and Motor Disturbances, Arch. Neurol. & Psychiat. **20**:720-730 (Oct.) 1928. Chaney, L. B., and McGraw, M. B.: Reflexes and Other Motor Activities in Newborn Infants, Bull. Neurol. Inst. New York **2**:1-56 (March) 1932.

26. Irwin, O. C.: The Amount and Nature of Activities of Newborn Infants Under Constant External Stimulating Conditions During the First Ten Days of Life, Genetic Psychology Monographs, Worcester, Mass., Clark University Press, 1930, vol. 8, no. 1, pp. 1-92. Irwin, O. C., and Weiss, A. P.: A Note on Mass Activity in Newborn Infants, Pedagog. Semin. & J. Genetic Psychol. **38**:20-30 (Dec.) 1930. Dennis, W.: The Rôle of Mass Activity in the Development of Infant Behavior, Psychol. Rev. **39**:593-595 (Nov.) 1932. Gilmer, B. von H.: An Analysis of the Spontaneous Responses of the Newborn Infant, Pedagog. Semin. & J. Genetic Psychol. **42**:392-403 (June) 1933.

27. This description follows in part that of Gesell and of Shirley.

ments. Concurrently, motor control spreads out from the shoulders to the upper extremities; the infant exhibits increased ability to extend the arms and the forearms, and the activity is not confined solely to the lateral and midline planes of the body. In the meantime, concomitant postural developments and adjustments are evidenced in the pelvis and the lower extremities. Early, the legs are flexed at the hips and knees, and these attitudes are followed by extension movements and the onset of crawling activities. Crawling may be distinguished from creeping in that the abdomen touches the platform in crawling, whereas in creeping locomotion takes place on the hands, knees and legs. Certain rolling phenomena from the prone to the supine position or the

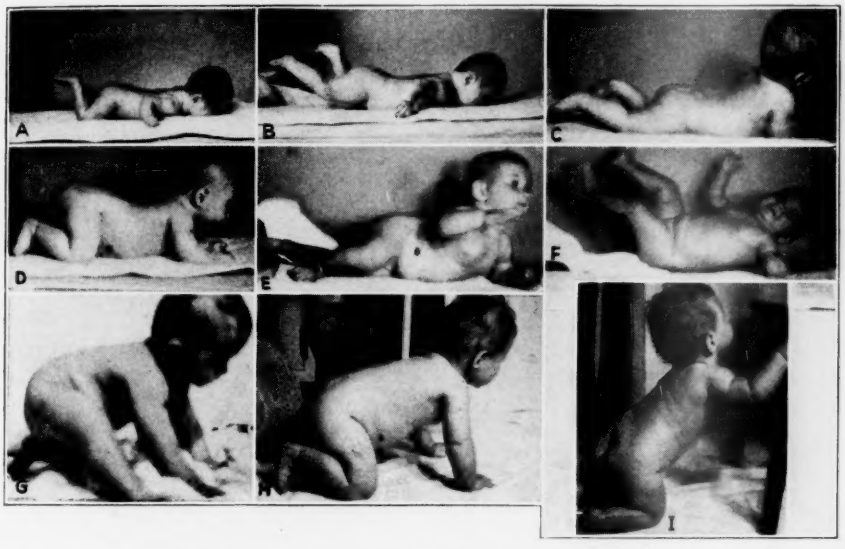

Fig. 1.—Selected phases in the sequence of postural and locomotor development which illustrate the progress of growth from the time the baby is in the early prone fetal position of the new-born infant until he is able to pull himself up to standing, in later infancy.

reverse are then seen, as well as pivoting movements clockwise or counterclockwise. With the assumption of the quadruped position, creeping activities begin, and one phase of locomotion is accomplished. At times, movement may occur in the "all fours position," an activity due either to a regressive form of behavior or to a transitional stage between creeping and walking.[28] Shirley [29] summarized the stages in

28. Hrdlička, A.: Children Who Run on All Fours and Other Animal-Like Behaviors in the Human Child, New York, McGraw-Hill Book Company, 1931. Levy, D. M., and Tulchin, S. H.: On the Problem of "All Fours" Locomotion, Pedagog. Semin. & J. Genetic Psychol. **47**:193-203 (Sept.) 1935.

29. Shirley,[19] pp. 44-52.

the creeping sequence as follows: fetal position, lifting up the head, chin up, chest up, drawing up the knees, swimming and rolling movements, hitching movements on the back, some progress in the prone position, the "suspension bridge" reaction, scooting backward, creeping and hitching.

Returning again to the new-born infant, I shall trace the developmental steps with the baby in the supine, or dorsal, position (fig. 2). During the early phases, activity of the head is restricted to rotation to either side and back to the midline, the infant being unable to lift

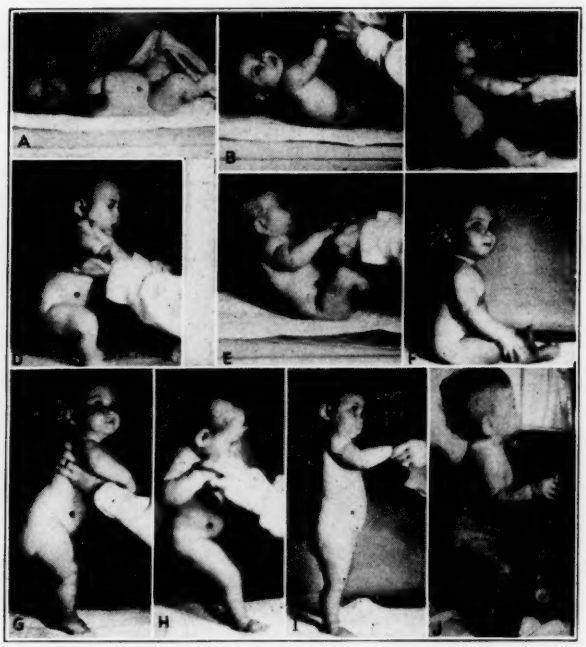

Fig. 2.—Photographs illustrating certain stages in the growth of postural and locomotor traits from the time the baby is in the early supine position of the new-born infant until he pulls himself up to standing, in later infancy.

the weight of his head against gravity. If the baby is pulled up by the arms, the head drops back. Later this difficulty is overcome, and lifting of the head occurs, as well as compensatory raising movements of the shoulders, as a postural adjustment preliminary to the assumption of the sitting position. Early, when the infant is pulled up to a sitting posture, the trunk leans forward and the head is wobbly, but later the back straightens and the control of movements of the head improves. The support of the body may be shifted from the armpits to the ribs and then to the abdomen, until the baby is finally able to

sit up alone. The latter phase of motor control is abetted by the acquisition of motor coordination of the arms and forearms and is dependent on the onset of extension movements and the increase in the radius of exploration of all planes about the body, beginning with the regions of the head and face and spreading down to the chest and abdomen and finally below the waist line to the feet. Meanwhile, motor control spreads down through the trunk with the appearance of rolling movements to either side, an activity accompanied by turning of the head and shoulders. Arching of the back and bouncing movements at the hips also occur, with a concurrent increase of kicking movements of the lower extremities. When held erect, the infant exhibits characteristic pushing and stepping activities of the feet. With the support which is achieved by the use of the upper extremities and increased control of the feet, upright reactions proceed from standing with help, pulling himself up and climbing to stand, until the child is able to stand

Fig. 3.—The sequence from the phase of standing holding on to furniture to that of walking alone.

up alone. These reactions are followed by walking with support or holding on until independent walking occurs (fig. 3). Gesell and his co-workers [30] emphasized the fact that the accomplishment of the erect posture is a complicated form of behavior involving many preparatory stages and summarized the developmental sequence as follows: supine position, assisted sitting, stepping when held in suspension, independent sitting, supporting weight when held, pulling self up to standing, supporting weight with physical prop, cruising, standing momentarily, independent standing, independent steps, toddling, walking and running. Shirley [31] and Burnside [32] called attention to the sequence of significant

30. Gesell, Thompson and Amatruda,[18] p. 97.

31. Shirley,[19] pp. 94-97.

32. Burnside, L. H.: Coordination of Locomotion in Infants, Genetic Psychology Monographs, Worcester, Mass., Clark University Press, 1927, vol. 2, no. 5, pp. 284-372.

stages in the development of walking. At first speed increases slowly, when babies are led; then acceleration occurs, with walking alone. There is also a gradual increase in the length of the step, and the earlier greater width of the step is decreased when the child walks alone, as are the width of the stepping base and the stepping angle.

Shirley [33] classified the successive phases of motor development into dynamic orders of skills, passive postural control being distinguished from active efforts at locomotion. In summarizing the significance of the orders of skills in relation to the general pattern of postural and locomotor development, she [34] stated:

> The development of motor skills is not haphazard but follows an orderly plan: first, the baby attains postural control of the upper trunk region; second, his postural control moves downward to include the entire trunk region and in addition exhibits random activity little directed toward locomotion; third, he makes active and vigorous efforts at locomotion, but his poorly co-ordinated movements meet with only slight success; fourth, postural control of the entire body becomes complete, and the baby achieves locomotion by the two or three methods; and fifth, postural control and co-ordination are combined and he reaches the goal of walking, toward which all his development has been tending. This represents the *pattern* of motor development. The sequence is simple and logical rather than elaborate and detailed. In its broad aspects the pattern is inflexible, but in its detail it is modifiable to suit the individual capacities of each baby.

MATURATION OF THE CENTRAL NERVOUS SYSTEM

The sequence in the pattern of motor development is readily observed in daily routine clinical examinations. However, the explanation of the basis for the regularity in its occurrence is still a problem open to investigation. A vast and widely scattered literature has accumulated on this phase of somatic development, which is assuming growing importance in the estimation of the early trend of progress of the maturing infant and child. It was deemed worth while, therefore, to review certain of the more important investigations on the relationship between physical and somatic behavioral growth. Perhaps evidence of value could be found in studies on the maturation of the nervous system to account for the sequence in the growth of postural and locomotor traits. At the outset it should be emphasized that no attempt is being made to build up a synthetic concept in explanation of the motor sequence. On the contrary, cognizance will be taken at all times of the structural and functional unity of the total organism and of the organismal patterns of behavior, by which growth proceeds generally from the whole to the parts. Attention will therefore be directed toward an analysis of the various components comprising the intricate systems.

33. Shirley,[19] pp. 101-104.
34. Shirley,[19] p. 103.

CEPHALOCAUDAL DEVELOPMENT

In describing the early growth of the central nervous system, Jackson [35] and Kingsbury [36] stressed the fact that growth and differentiation of a great portion of the body proceed in a wavelike manner from head to tail. This mode of development holds true not only for the somites but equally for structures that are formed from them. In general, development in the vertical axis of the body appears first in the head region and progresses toward the tail. Similarly, in the transverse plane development begins in the mid-dorsal region and progresses latero-ventrally and in the limbs proximodistally. This method of growth is of probable importance phylogenetically, for the head is the most primitive portion of the body and is therefore precocious in development, whereas the trunk is perhaps a secondary acquisition arising as an extension of the primitive head region. Anteroposterior development thus leads to definite formation of a head and centralization of the nervous system, the front end of which becomes enhanced in importance and forms a brain, which assumes a dominant influence over the more caudal segments.

In the opinion of Kingsbury,[37] this mode of growth has far reaching significance in developmental transformation, particularly with respect to human morphology. Long familiar to biologists, it has been designated by such convenient phrases as the "law of antero-posterior development" and the "law of cephalocaudal direction," the terms of course revealing "nothing more than the time sequence of developmental events." However, the head to tail sequence in the development of the nervous system is highly suggestive as a significant factor with respect to the subsequent head to tail development of postural and locomotor activities of the organism.

PHYSIOLOGIC GRADIENTS

According to Child,[38] the law of anteroposterior development merely recognizes the existence of metabolic gradients or excitation-transmission phenomena along the main axes of the organism during

35. Jackson, C. M.: Morphogenesis, in Morris, H.: Human Anatomy, edited by C. M. Jackson, Philadelphia, P. Blakiston's Son & Co., 1914, pp. 12, 13 and 24.

36. Kingsbury, B. F.: The Significance of the So-Called Law of Cephalocaudal Differential Growth, Anat. Rec. **27**:305-321, 1924.

37. Kingsbury, B. F.: On the So-Called Law of Antero-Posterior Development, Anat. Rec. **33**:73-87, 1926.

38. Child, C. M.: The Origin and Development of the Nervous System from a Physiological Point of View, Chicago, University of Chicago Press, 1921, pp. 1-23; Senescence and Rejuvenescence, Chicago, University of Chicago Press, 1915, p. 204.

the period of development. The gradients consist of a hierarchy of differences in the degree of fundamental protoplasmic activity and refer to the rate of metabolism, particularly to the rate of oxidation. They are not the cause of growth and differentiation, nor are they determinants of the nature of the developing organ. The gradients represent merely certain physiologic conditions in which protoplasm gives rise to the order of a pattern, the axial or axial-symmetrical. The establishment of physiologic gradients, or "lines of diminishing intensity of vital reaction," as they have been called by Herrick,[39] determines the existence of the mechanisms of dominance and subordination. The high, or more irritable and active, end of the gradient becomes physiologically dominant over all the limbs of the gradient within a range of distance depending on the intensity of activity of the dominant region and the conductivity of the medium. In like manner, any level of the gradient controls in greater or lesser degree more posterior levels.

The central nervous system, Child stated, thus develops on the physiologic basis of excitation-transmission gradients, which constitute the integrating factor of the organism and form the basis of polarity and symmetry. The gradient is the primary behavior mechanism of the axial type and the physiologic foundation on which the axial pattern is built.[40] Primary gradients may persist throughout life or may undergo modification during the course of development, with the establishment of secondary gradients. They are not independent of external factors but are the result of the differential action of such factors on the general rate of protoplasmic activity. The sequence of events is definite and orderly and even in the fully developed organism the pattern may show marked relation to the primary gradient.

METABOLIC GRADIENTS

Further evidence of the existence of a hierarchy of graded activity in the central nervous system may be gleaned from metabolic studies on excised portions of brain tissue from animals and human beings. In 1904 Herter [41] showed by the injection of methylene blue into the blood stream of animals that the organic dye was rapidly reduced by the

39. Herrick, C. J.: Neurological Foundations of Animal Behavior, New York, Henry Holt & Company, Inc., 1924, p. 9.

40. Child, C. M.: Physiological Foundations of Behavior, New York, Henry Holt & Company, Inc., 1924, p. 227; Behavior Origins from a Physiologic Point of View, Arch. Neurol. & Psychiat. **15**:173-184 (Feb.) 1926.

41. Herter, C. A., and Richards, A. N.: The Influence of Chloroform on Intravital Staining with Methylene Blue, Am. J. Physiol. **12**:207-212 (Oct.) 1904-1905. Herter, C. A.: The Influence of Fever on the Reducing Action of the Animal Organism, ibid. **12**:457-465 (Jan.) 1904-1905.

brain, indicating a considerable utilization of oxygen. In 1917 MacArthur and Jones [42] conducted a systematic study of the respiratory metabolism of the central nervous systems of mammals, using ground brain tissues of guinea-pigs, calves and old cows and testing them manometrically for total oxygen consumption and carbon dioxide elimination. Graded differences were found in the oxidation rates of various divisions of the central nervous system, in order from greater to lesser activity as follows: cerebrum, cerebellum, midbrain, medulla, corpus callosum, spinal cord and nerve. The investigators also demonstrated that cerebral gray matter consumed about twice as much oxygen as did white matter and that only about two-thirds as much carbon dioxide was produced by the latter. The subsequent observations of MacArthur and Doisy [43] on samples of brain tissue from human fetuses, young infants and adults also showed the dominance of the central nervous system in the regulation of the metabolic activities of the organism.

The aforementioned studies were confirmed much later by the work of Holmes,[44] who extended his generalizations to include the peripheral nervous system, and by the more recent investigations of Wortis.[45] Mention should be made of the studies by Hoagland,[46] which call attention to the existence of the continuous master mechanisms or pacemakers controlling many aspects of conduct of the organism. Hoagland expressed the opinion that many of the overt response patterns of the organism are determined by the interaction of chemical events within cells and groups of cells, a fact which has for the most part been overlooked in studies on the genesis of behavior.

MYELINIZATION

An additional process of significance in the maturation of the nervous system merits consideration in relation to its probable influence on the orderly sequence in postural and locomotor development. One of the important phases of growth in the nervous system is myelinization, a study of which is valuable in the attempt to correlate the

42. MacArthur, C. G., and Jones, O. C.: Some Factors Influencing the Respiration of Ground Nervous Tissue, J. Biol. Chem. **32**:259-274 (Nov.) 1917.

43. MacArthur, C. G., and Doisy, E. A.: Qualitative Changes in the Human Brain During Growth, J. Comp. Neurol. **30**:445-470 (Aug.) 1919.

44. Holmes, E. G.: Oxidations in Central and Peripheral Nervous Tissue, Biochem. J. **24**:914-925, 1930.

45. Wortis, S. B.: Respiratory Metabolism in Excised Brain Tissue: I. Respiratory Quotient; Carbohydrate and Lactic Acid Utilization, Am. J. Psychiat. **13**:725-732 (Jan.) 1934.

46. Hoagland, H.: Pacemakers in Relation to Aspects of Behavior, Experimental Biology Series, New York, The Macmillan Company, 1935.

development of somatic and reflexive behavior with the maturation of the nervous system. The classic researches of Flechsig, in 1876,[47] opened up a fertile field of investigation. According to Tilney and Casamajor,[48] he was probably the first to suggest that the development of the nervous system could be traced by ascertaining the periods at which the various nerve fibers acquire myelin sheaths.

In general, nerve tracts acquire myelin sheaths in the same order in which they develop, the coverings being demonstrable early in fiber systems which are phylogenetically the oldest and in those becoming functional first. Regions receiving myelin sheaths early are the centers of lower functions, whereas the later medullating areas are the seats of highest intellectual functions.[49] Medullation begins in the human central nervous system about the fourth or fifth month of intra-uterine life, but not in all portions at the same time or simultaneously in all parts of a single fiber.[50] In the spinal cord, ventral roots are myelinized before dorsal roots, and the process appears first in the cervical portion of the cord and proceeds caudally. In the brain proper the spread is cephalad, the medulla and the midbrain showing the first evidences of myelinization. At birth, Pfister stated,[51] the spinal cord possesses practically its full measure of myelin constituent, whereas the brain stem, the cerebellum and extensive areas of the cerebral cortex are devoid of it. In full term infants, fiber tracts are provided with myelin sheaths that are subservient to general sensibility, tactile and muscle sense, with the pyramidal tracts being also partly invested, the process continuing until the beginning of puberty and probably somewhat later.[52]

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47. Flechsig, P.: Die Leitungsbahnen im Gehirn und Rückenmark des Menschen, Leipzig, W. Engelmann, 1876; Meine myelogenetische Hirnlehre, Berlin, Julius Springer, 1927.

48. Tilney, F., and Casamajor, L.: Myelogeny as Applied to the Study of Behavior, Arch. Neurol. & Psychiat. **12**:1-66 (July) 1924.

49. Ladd, G. T., and Woodworth, R. S.: Elements of Physiological Psychology, New York, Charles Scribner's Sons, 1911, pp. 58, 223 and 246.

50. Growth and Development of the Child: I. General Considerations; II. Anatomy and Physiology, White House Conference on Child Health and Protection, New York, D. Appleton-Century Company, 1933, pp. 186-190 and 210-216. Langworthy, O. R.: The Development of Behavior Patterns and Myelinization of Tracts in the Nervous System, Arch. Neurol. & Psychiat. **28**:1365-1382 (Dec.) 1932.

51. Pfister, H.: The Peculiarities of the Child's Nervous System, in von Pfaundler, M., and Schlossman, A.: The Diseases of Children, Philadelphia, J. B. Lippincott Company, 1912, vol. 4, pp. 121-132.

52. Tilney, F., and Riley, H. A.: The Form and Functions of the Central Nervous System, New York, Paul B. Hoeber, Inc., 1921, pp. 188 and 677.

Although there has been considerable discussion [53] as to the significance of the rôle played by medullation in the maturing nervous system with respect to the development of behavior, the data are highly suggestive of an intimate relationship. The process of myelinization shows a well organized sequence proceeding from phylogenetically older pathways, which control more primitive types of behavioral patterns, to the pathways of more recent acquisition, which control activities of increasing complexity in the general scale of reactions.

POSTNATAL MATURATION OF THE NERVOUS SYSTEM

In the postnatal growth of the organism certain salient features predominate which exert a marked influence on the future development of behavior in infancy. The work of Scammon [54] and of Wetzel [55] has shown that early postnatal growth is marked by a differential rate of accretion by the various tissues of the body, a growth that is characterized by sudden change in velocity toward either acceleration or retardation. These comparative changes in rhythm have been graphically represented by Scammon (fig. 4). Of particular interest is the neural type of maturation as represented in the brain, the growth curve showing an early and rapid postnatal rise during the first few years of life, with a negative acceleration and leveling off at about the time between puberty and maturity. This phase of development is succeeded by the differentiation of nerve tissue and slower rates of growth for certain parts of the nervous system. The considerable growth of the brain during the first year of life is shown in figure 5. During the intra-uterine period the growth of tissue proceeds at a more uniform rate and, according to Scammon, may be represented graphically by a straight line. After birth the modes change and the growth curve becomes curvilinear, the form depending on the inherent velocity of the organ. Again the early rapid growth of the nervous system is evident; it is exceeded only by that of the trunk. The details with reference to the intrinsic growth of the nervous system and its subdivisions have been adequately described by Scammon [56] and by Stiles [57] and need not be described here. It will

53. Angulo y González, A. W.: Neurological Interpretation of Fetal Behavior: The Motor Cell Columns of the Albino Rat Before Birth, Anat. Rec. **42**:17, 1929; Is Myelogeny an Absolute Index of Behavioral Capacity? J. Comp. Neurol. **48**: 459-464, 1929.

54. Scammon, R. E.: The Measurement of the Body in Childhood, in Harris, J. A.; Jackson, C. M.; Paterson, D. G., and Scammon, R. E.: The Measurement of Man, Minneapolis, University of Minnesota Press, 1930, pp. 173-215.

55. Wetzel, N. C.: On the Motion of Growth: Prologomena to the Clinical Study of Human Growth and Metabolism, J. Pediat. **3**:252-264 (July) 1933.

56. Scammon, R. E.: A Summary of the Anatomy of the Infant and Child, in Abt, Isaac A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 1, pp. 257-444.

(Footnotes continued on next page)

suffice to state that its development is characterized by constant change of form microscopically as well as grossly, until typical adult features are acquired. In this connection, the importance of subsequent micro-

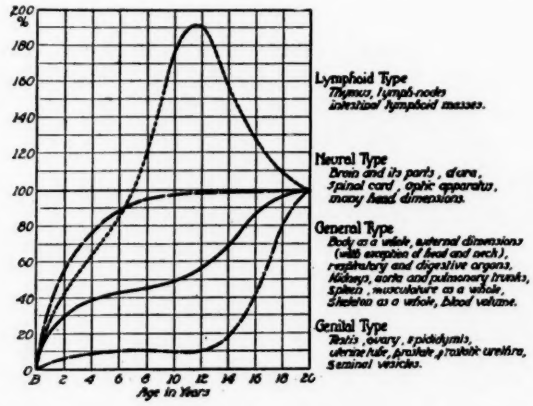

Fig. 4.—Major types of postnatal growth. (From Scammon, R. E.: The Measurement of the Body in Childhood, in The Measurement of Man, Minneapolis, University of Minnesota Press, 1930, p. 103; reproduced by permission of the publishers.)

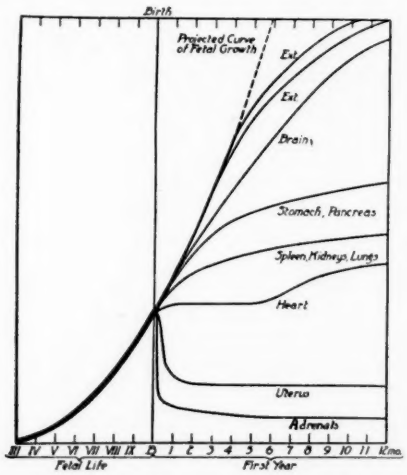

Fig. 5.—Differentiation of the various types of growth during the first year of life, as contrasted with the simple type of growth curve of the fetal period. (From Scammon, R. E.: The Measurement of the Body in Childhood, in The Measurement of Man, Minnesota, University of Minnesota Press, 1930, p. 205; reproduced by permission of the publishers.)

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57. Stiles, P. G.: The Physiology of the Nervous System in Early Life, in Abt, Isaac A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1925, vol. 7, pp. 1-25.

scopic changes in structure should be borne in mind, as even minute changes in formed structures may have a profound effect on the development of behavior.[58]

CONCOMITANT POSTNATAL MOTOR DEVELOPMENT

The significance of the foregoing data with reference to the genesis of motor development and of behavior in general lies in the fact that one is dealing not only with an immature organ but also with an inadequate organ which is physiologically active only in part and in which substantial alterations occur until the time of full maturity.[51] It should be borne in mind that the nervous system is the chief means whereby the various structures of the body are brought into harmonious functional relationships and whereby the organism is brought into contact with its environment.[59] Lashley [60] stressed the mutual dependence of parts rather than the specialization of structure in the growth of behavior of the organism.

Accompanying the early rapid postnatal physical alterations in the nervous system, changes in motor development proceed at a remarkable pace, and the total pattern is constantly reorganized along new lines. Goodenough [61] expressed the belief that the changes occur as a result of rapid improvement in functions already manifest at birth, the concomitant appearance of many new items of behavior, the differentiation of movements of local parts from the mass random movements of the infant and, to some extent, the recombination of various local movements. At any rate, there is evident the rapid change from the early, coarse motor phenomena of the new-born infant to the later coordinated and complex activities of the older child. In addition, Goodenough emphasized the fact that although changes in behavior proceed with great rapidity they are not haphazard in their manner of appearance, the successive changes in motor development being characterized by a remarkable orderliness as to time and pattern regardless of the individual rate of development.

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58. Coghill,[9] p. 84. Donaldson, H. H., and Nagasaka, G.: On the Increase in the Diameters of Nerve-Cell Bodies and of the Fibers Arising from Them During the Later Phases of Growth (Albino Rat), J. Comp. Neurol. **29**:529-551, 1918.

59. Sherrington, C. S.: The Integrative Action of the Nervous System, London, Constable & Co., Ltd., 1906, p. 2.

60. Lashley, K. S.: Integrative Functions of the Cerebral Cortex, Physiol. Rev. **13**:1-42 (Jan.) 1933.

61. Goodenough, F. L.: Developmental Psychology, New York, D. Appleton-Century Company, 1934, pp. 158-179.

The following statement of Wetzel [55] with respect to his observations on the motion of physical growth applies perhaps equally well to the developmental rhythm, or cycle of behavior:

> Succeeding birth, we are wont to observe a young subject develop as the process of growth unfolds itself, and always to do so no doubt with a considerable and humble amazement at the regularity, and one may even add, at the biologic precision with which familiar landmarks are reached and passed.

MATURATION AND LEARNING

It must not be construed that the factors of learning and of practice are being minimized in an attempt to analyze the development of motor activity in terms of its structural and operational components. It is fully realized that lapse of time without practice tends to lower the fixation value of a function or to cause a loss in the learning process. However, the weight of evidence appears to favor the point of view that maturation plays the dominant rôle in initiation of the development of basic motor skills, with learning assuming only a secondary part in their subsequent perfection in the attainment of greater accuracy, speed, adaptability and strength through practice effects on the elements of the acts.

In summarizing the common factors in maturational development, Stone [62] stated that the anlagen of fundamental behavioral patterns are laid down in the central nervous system during embryonal and fetal development and continue their maturation until functional maturity is attained, no practice whatever being required to initiate first embryonal movements. Subsequent development, with individuation of responses, proceeds without practice until the adult stage of growth is reached. Stone added that learning is essentially a secondary elaboration of maturational development. The primary or basic regulators of maturation are endogenous and are determined by hereditary mechanisms,[63] whereas learned responses are not transmitted as heritable characters. This opinion is also concurred in by Lashley,[64] as a result of his work on animals. The observations on identical twins by Gesell and Thomp-

62. Stone, C. P.: Learning: I. The Factor of Maturation, in Murchison, C. A.: Handbook of General Experimental Psychology, Worcester, Mass., Clark University Press, 1934, pp. 352-381.

63. Morgan, T. H.: The Mechanisms and Laws of Heredity, in Murchison, C. A.: Handbook of General Experimental Psychology, Worcester, Mass., Clark University Press, 1934, pp. 109-154.

64. Lashley, K. S.: Learning: III. Nervous Mechanism in Learning, in Murchison, C. A.: Handbook of General Experimental Psychology, Worcester, Mass., Clark University Press, 1934, pp. 456-496.

son [65] and the experiments on animals by Shepard and Breed,[66] Moseley,[67] Carmichael [68] and Bird [69] also stress the factor of the growth of the nervous system in relation to maturation in somatic patterns of behavior.[69a]

In this connection, Shirley [70] presented a cogent argument in favor of the maturation theory in calling attention to the fact that the general pattern of motor development was the same even before the advent of present day methods of child training and conditioning, with their possibly modifying effects. The clinical observations of pioneer investigators were cited to substantiate this fact. In addition, Shirley expressed the belief that although individual differences could be accounted for perhaps on the basis of differences in the amount of practice, yet learning does not admit of the inherent orderliness in motor development, with its progress from cephalad to caudad. The effect of random effort would be haphazardness and reversal in the order of appearance of the various stages in motor growth, and the onset of each phase of activity would be gradual rather than sudden. The suddeness of appearance of the successive phases of motor development is well recognized by clinicians and by the laity. It should also be noted that if motor development were primarily dependent on learning it would be difficult to conceive how the pattern could be basically the same in its sequence for all organisms of the species living under totally different environments, with variable and unequal opportunities for training. Such a concept would fallaciously predicate a universal homogeneity of environmental influences.

65. Gesell, A., and Thompson, H.: Learning and Growth in Identical Infant Twins, Genetic Psychology Monographs, Worcester, Mass., Clark University Press, 1929, vol. 6, no. 1, pp. 1-123.

66. Shepard, J. F., and Breed, F. S.: Maturation and Use in the Development of an Instinct, J. Animal Behavior **3**:274-285 (July-Aug.) 1913.

67. Moseley, D.: The Accuracy of Pecking Response in Chicks, J. Comp. Psychol. **5**:75-97 (Feb.) 1925.

68. Carmichael, L.: The Development of Behavior in Vertebrates Experimentally Removed from Influence of External Stimulation, Psychol. Rev. **33**:51-58 (Jan.) 1926.

69. Bird, S.: The Effect of Maturation upon the Pecking Instincts of Chicks, Pedagog. Semin. & J. Genetic Psychol. **33**:212-234 (June) 1926.

69a. Carmichael recently suggested, basing his idea on an analysis of the relationship between external stimulation and internal growth in the development of behavior, that since the changes arising from processes of inner growth (maturation) are physiologically similar to those resulting from external stimulation (learning), the terms maturation and learning be abandoned and replaced by descriptive empirical curves representing changes in behavior measured by time (Carmichael, L.: A Re-Evaluation of the Concepts of Maturation and Learning as Applied to the Early Development of Behavior, Psychol. Rev. **43**:450-470 [Sept.] 1936).

70. Shirley,[19] pp. 182-195.

PRACTICAL CONSIDERATIONS

An understanding of the significance of the phenomena of motor development in its relationship to the morphology of the central nervous system is of importance in the clinical observation of the infant and child, particularly during the first two years of life. Examination of the test items of normal developmental schedules during that period will reveal that they deal predominantly with motor characteristics, since abstract forms of behavior are not sufficiently developed during the first two years to be of significant diagnostic value. Wellman [71] stated that "motor acts are intrinsic parts of the measures of mental development." The growth of postural and locomotor traits and of manipulatory motor acts and the so-called acts of motor play is the most readily observed and the most easily measured part of the child's repertory of behavior and serves as a valuable indicator in the estimation of the rate and tempo of development.

As has been indicated by the work of Smith [72] and of Borgiotti,[73] as well as by the studies of Hess, Mohr and Bartelme [74] on premature infants, a knowledge of the basic pattern of motor development is of value not only in the study of the healthy infant but also, from a diagnostic and prognostic point of view, in cases of disease. In a previous publication [75] some of the factors in disease were weighed in their relationship to motor development. Such predisposing influences were considered as constitution, individual and group immunity and susceptibility to disease and racial differences, as well as age, sex, season and climate. In addition, the more direct effects of disease were evaluated, its severity, duration and frequency of occurrence in the child. It was found that the growth of motor traits is subject to the operation of many influences, each of which may induce varying degrees of abnormal deviation during disease by altering adversely the normal course of maturation of the various structural and functional systems of the body, the nervous system in particular. In the infant, with the rapid changes occurring in the form and structure of the nervous system,

71. Wellman, B. L.: Physical Growth and Motor Development and Their Relation to Mental Development in Children, in Murchison, C. A.: Handbook of Child Psychology, Worcester, Mass., Clark University Press, 1931, pp. 242-277.

72. Smith, S.: The Influence of Illness During the First Two Years on Motor Development, Pedagog. Semin. & J. Genetic Psychol. **39**:284-287 (June) 1931.

73. Borgiotti, G. C.: Reazioni motorie di raddrizzamento nella prima infanzia, Riv. di clin. pediat. **31**:533-551 (May) 1933.

74. Hess, J. H.; Mohr, G. J., and Bartelme, P. F.: The Physical and Mental Growth of Prematurely Born Children, Chicago, University of Chicago Press, 1934, pp. 121-182.

75. Abramson, H.: The Influence of Disease on Motor Development During Childhood, Psychol. Bull. **31**:800-814 (Dec.) 1934.

disease processes may be sufficient to cause profound and irreparable damage. The permanent character of lesions in certain areas of the central and peripheral nervous systems is well known. In this connection it is of interest to recall the clinical observation that the behavior of persons whose nervous systems are damaged by disease tends to revert to more primitive characteristics. However, as has been pointed out by Gesell,[76] the basic pattern of motor development remains the same, for the maturation of the nervous system proceeds toward the optimum in unimpaired areas. Gesell said:

> It is for this reason that certain clinical types of profound motor disability attain none the less considerable approximation to normality in certain patterns of behavior.

SUMMARY

In the development of the human infant, most outstanding and certain in its general course is the progressive unfolding of postural and locomotor traits. From the primitive but highly significant manifest diffuse reactions of the new-born baby to the subsequent latent coordinated activities of the maturing infant, the development of the system of motor conduct reveals a purposive plan, purposive not in the teleologic sense but from the point of view of utility for the organism. It is a development exhibiting a progressive emergence of graded skills of increasing complexity in the general scale of somatic behavior, manifesting an organized sequence of related antecedent and consequent events in a temporal series and representing a movement of growth from the whole to parts or from fundamental to accessory. This advancement of growth is logical and regular in its serial order, being governed apparently by biologic laws strikingly similar to those controlling the logical course of physical growth. Just as in physical development growth spreads downward from the cephalic end of the organism in a caudal direction, similarly in the development of basic motor skills control migrates down through the body from head to tail, with a concurrent spread of coordinaion out to the extremities.

In an attempt to ascertain the structural and operational factors contributing to the sequence in motor development, the literature was reviewed, and it revealed that certain predominant features in the growth of the central nervous system probably have an intimate bearing on the development of the motor pattern. Consideration of the early maturation of the nervous system showed its growth to be in accordance with the law of cephalocaudal development, with growth proceeding in a wavelike manner from head to tail. The significance of that mode of differentiation involved in turn the operation of metabolic gradients

76. Gesell, A.: Maturation and Infant Behavior Pattern, Psychol. Rev. **36**: 307-319 (July) 1929.

along the main axis of the organism, the gradients giving rise to the order of a pattern, the axial or axial symmetrical, and representing, furthermore, the integrating factor of the individual organism and the general physiologic foundation on which the axial pattern is built.

In addition, the significance of the rôle of myelinization in the maturation of the central nervous system was considered. This process shows a well organized sequence proceeding from phylogenetically older pathways, which control more primitive types of behavior, to pathways of more recent acquisition, which control activities of increasing complexity in the general scale of reactions. Of added importance are the features characterizing the early rapid postnatal growth of the central nervous system, with its continual change in form and structure until maturity. Paralleling the physical alterations in the developing nervous system, changes in motor behavior proceed at a remarkable rate, with the total pattern being constantly reorganized along new lines. The weight of evidence appears to favor the view that the maturation of the nervous system plays the dominant rôle in initiating the development of basic motor skills and that learning assumes only a secondary part in their subsequent elaboration and perfection. To be sure, the significance of the relative rôles played by the various interrelated developmental mechanisms of the central nervous system either singly or in combination in the total growth pattern of the motor sequence is a problem still open to investigation.

In conclusion, it should be stated that a knowledge of the basic pattern of motor behavior is of value in estimating the rate and tempo of development of the infant and child not only during health but also during disease, the influences of which may induce varying degrees of abnormal deviation by altering adversely the normal course of maturation of the central nervous system.

1097 Madison Avenue.

News and Comment

GENERAL

Physicians Certified by American Board of Pediatrics.—The following physicians have been certified by the American Board of Pediatrics since the last report:

William Bradford Adams, Springfield, Mass.; Ben Benjamin, Montreal, Canada; Claude McKinley Burpee, Augusta, Ga.; Iris M. Chamberlain, Chicago; Forris Ensor Chick, New York; Harry Eron Cohen, New York; Walter R. Coles, Brooklyn; Reuben Arthur Craig, Kokomo, Ind.; Hugh Jefferson Davis, Washington, D. C.; William E. Donahoe, Sioux Falls, S. D.; Louis M. Earle, Hollywood, Calif.; George H. Garrison, Oklahoma City; George Ketcham Hagaman, St. Paul; Lawrence Vance Hanlon, Brooklyn; Henry P. Harrell, Augusta, Ga.; Norman Louis Hawkins, Watertown, N. Y.; F. G. Hedenstrom, St. Paul; Julius Heilbrunn, Jersey City, N. J.; Lewis D. Hoppe Jr., Atlanta, Ga.; John Taylor Howell Jr., New York; Francis Rush Janney, Wauwatosa, Wis.; Newell Jones, Hollywood, Calif.; J. N. Lande, Sioux City, Iowa; John Fitch Landon, New York; Richard A. Lawrence, Albany, N. Y.; Abel Lax, Montreal, Canada; William Ray Little, Trenton, N. J.; Norman M. Macneill, Philadelphia; Thomas Juett Marshall, Paducah, Ky.; William Charles McGuire, New Haven, Conn.; William Baird McIlwaine, Petersburg, Va.; John M. Mitchell, Evanston, Ill.; Oscar A. Mockridge, Montclair, N. J.; Fred Moore, Des Moines, Iowa; Harold A. Murray, Newark, N. J.; Kenneth D. Nichol, Brooklyn; Roland Edward Nutting, Duluth, Minn.; Thomas E. Oast, Portsmouth, Va.; William Francis O'Donnell, Washington, D. C.; Lawrence Francis Richdorf, Minneapolis; William Rosenson, New York; Joseph Carr Savage, Los Angeles; R. Hunter Scott, Newark, N. J.; Harry A. Spigel, Washington, D. C.; Frank E. Stevenson, Cincinnati; Alexander Stewart, St. Paul; Lucy Porter Sutton, New York; Edward Sheppard Thorpe Jr., Philadelphia; Harmon Tremaine, Boise, Idaho; Thomas Edward Waldie, New York; Walter F. Watton, Brooklyn; Robert Lawson Wilder, Minneapolis; LeRoy A. Wilkes, Trenton, N. J.; James R. Wilson, Syracuse, N. Y.

None of these physicians were examined.

Camp for Diabetic Children.—In the summer of 1936 the New York Diabetic Association of the New York Tuberculosis and Health Association, Inc., established one of the first summer camps for diabetic children. It was made possible through private contributions, the first of which was given by Mr. Lucius N. Littauer.

The camp was open for eight weeks and accommodated four groups of seven or eight children each. Each group stayed two weeks. The operating cost was approximately $3.69 per child per day. It was felt that each child received definite benefit from his stay in camp, and it is hoped that in the future the camp may be continued and that each child may be given the privilege of four weeks in camp instead of two.

Fourth International Pediatric Congress.—The Fourth International Pediatric Congress will be held in Rome, Italy, September 27 to 30.

American Board of Pediatrics.—The American Board of Pediatrics will hold examinations as follows:

At Los Angeles, during the meeting of Region IV of the American Academy of Pediatrics the latter part of October.

At Chicago, during the meeting of Region III of the American Academy of Pediatrics Nov. 4, 5 and 6.

At Boston, during the meeting of Region I of the American Academy of Peliatrics Nov. 12 and 13.

At New Orleans, during the joint meeting of Region II of the American Academy of Pediatrics and the Southern Medical Association Nov. 30 and Dec. 1, 2 and 3.

Definite dates for these examinations will be published later.

SOCIETY NEWS

New England Health Education Association.—The New England Health Education Association will hold its twelfth annual meeting on June 4 and 5 at the Massachusetts Institute of Technology, Cambridge, Mass.

UNIVERSITY NEWS

The usual summer courses on child development and parent education will be given by the University of Iowa from June 14 to August 6.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

REACTION OF THE CONNECTIVE TISSUES TO LIPIDES AND OTHER FOREIGN BODIES. E. H. TOMPKINS, Am. J. Syph., Gonor. & Ven. Dis. **20**:22 (Jan.) 1936.

The article is summed up in the following conclusions:

1. The reaction of the connective tissues to many unrelated foreign bodies, including tubercle bacilli, is presented by the following sequence of events: (*a*) an early influx of polymorphonuclear cells, which subsides in a few days; (*b*) appearance of monocytes about three days after the injection; these quickly develop to great size and show great activity; (*c*) appearance of clasmatocytes about five days after the injection; (*d*) appearance of epithelioid cells and of transitional forms between them and both monocytes and clasmatocytes about eight days after the injection; (*e*) appearance of giant cells of both foreign body and epithelioid types about ten days after the injection.

2. Injection of lipids prepared from egg yolk and from brain into the connective tissues causes focal increases in the number of macrophages similar to those caused by injection of other foreign bodies. In contrast, however, to the macrophages in the latter case, which show degenerative changes, the cells in the areas into which the lipids have been injected become physiologically hyperactive and show no evidences of degeneration into epithelioid and giant cells.

3. These lipids are quickly removed from the areas of injection, and there is no residual modification of the tissues.

ROYSTER, University, Va.

A HEREDITARY DEFECT OF THE N AGGLUTINOGEN. V. FRIEDENREICH, Deutsche Ztschr. f. d. ges. gerichtl. Med. **25**:358, 1936.

In a proceeding involving a question of paternity Friedenreich encountered an apparent exception to the laws governing the inheritance of the agglutinogens M and N of Landsteiner and Levine. The mother's blood cells seemed to belong to type M and the child's to type N. The examination revealed that the mother had a very weak agglutinogen N in her blood cells. Forty-two other persons belonging to the family of this mother were tested, and thirteen were found to possess the weak N receptor. Friedenreich concludes that there are two types of N receptors, N_1 and N_2; N_1 is the more common and stronger agglutinogen, and dominant in its inheritance over N_2. Except for the exceeding rarity of occurrence of the agglutinogen N_2, this finding resembles in many respects the existence of two types of A receptors, A_1 and A_2, in human red blood cells.

WIENER, Brooklyn. [ARCH. PATH.]

THE DETERMINATION OF THE ICTERUS INDEX WITH CAPILLARY BLOOD. C. P. W. WANG and N. J. EASTMAN, Chinese M. J. **50**:53 (Jan.) 1936.

Wang and Eastman criticize the previous method of determining the icteric index with capillary blood, that of D. Davis, published in 1926, because of the difficulty of completing the determination with such a small amount of blood as one gets from a stab. Another reason is that errors occur with such a small bore in the tubing and in the sealing off of the tube by heat.

The authors have overcome the disadvantages of the Davis apparatus by substituting for the glass tubing two Sahli hemoglobin pipets and by adopting a simple technic. Puncture of the skin delivers 20 cu. mm. of blood, which is abundant for making the determination. The standard solution is 1:100 potassium bichromate; from this different dilutions are made. Concentrated sulfuric acid is added

to the stock solution to preserve the color. The methods are described in detail, as well as the results. With both serum and plasma, these methods give accurate determinations.

NEFF, Kansas City, Mo.

Metabolism; Infant Feeding; Milk and Other Foods

ON THE MECHANISM OF THE HEMATOPOIETIC ACTION OF COBALT. J. M. ORTEN, Am. J. Physiol. **114**:414 (Jan.) 1936.

The oral and the subcutaneous administration of cobalt to young and to adult albino rats, respectively, produce significant increases in the proportion of reticulocytes in the blood preceding the typical elevation in the concentration of pigment and erythrocytes.

The concentration of bilirubin in the serum of cobalt-treated adult rats is slightly greater than that in the serum of comparable controls.

These results indicate that the hematopoietic activity of cobalt is a result of an increase in the rate of formation of hemoglobin and erythrocytes and that a passive accumulation of red cells as a result of decrease in the rate of destruction of these cells does not occur.

NOURSE, Cleveland.

THE BLOOD SUGAR LEVEL AFTER ADMINISTRATION OF PILOCARPINE, ATROPINE, AND ACETYL CHOLINE. M. C. HRUBETZ, Am. J. Physiol. **114**:551 (Feb.) 1936.

In a study of the nervous factors involved in the control of the concentration of the sugar in the blood, specific stimulation of the autonomic nervous system by drugs was used, with the following results: Pilocarpine raises the blood sugar level; atropine lowers it; atropine prevents the rise caused by pilocarpine, and acetylcholine lowers the blood sugar level.

NOURSE, Cleveland.

FILTERABLE SERUM CALCIUM IN LATE PREGNANT AND PARTURIENT WOMEN, AND IN THE NEWBORN. M. ANDERSCH and F. W. OBERST, J. Clin. Investigation **15**:131 (Jan.) 1936.

The average values for filtrable serum calcium were found to be constant in eight nonpregnant, eighteen normal late pregnant and twenty-five parturient women and in twenty-five new-born infants.

FROM THE AUTHORS' SUMMARY.

Vitamins; Avitaminoses

THE CAROTENE AND VITAMIN A REQUIREMENTS OF CHILDREN. W. R. AYKROYD and B. G. KRISHNAN, Indian J. M. Research **23**:741 (Jan.) 1936.

In labor camps Aykroyd and Krishnan saw children with ocular changes such as dryness of the cornea, smokiness of the cornea and yellow patches on the conjunctivae. The children had been fed on a diet low in carotene. In all, there were 436 children, 27 per cent of whom had ocular changes. They had received from 454 to 785 micrograms of carotene daily. It is assumed that the daily requirement is above this.

SNELLING, Toronto, Canada.

OBSERVATIONS ON THE HEART RATE IN VITAMIN B_1 AND DEFICIENCY. G. SANKARAN and B. G. KRISHNAN, Indian J. M. Research **23**:747 (Jan.) 1936.

Pigeons and rats show slowing of the heart's action on a diet lacking in vitamin B. Guinea-pigs on a diet deficient in vitamin C have tachycardia.

SNELLING, Toronto, Canada.

DEMONSTRATION OF LATENT DYSTROPHY OF THE CRYSTALLINE LENS IN AVITAMINOSIS. C. G. MOURIQUAND and J. ROLLET, Compt. rend. Soc. de biol. **122:** 1118, 1936.

In scorbutic guinea-pigs corneal paracentesis induces within twenty-four hours minute foci of cloudiness in the lens, visible with the slit lamp. If the animals are then given vitamin C, the mottling disappears completely, but if the administration of the vitamin is delayed three days, the lesions tend to persist.

LEBENSOHN, Chicago. [ARCH. OPHTH.]

INQUIRY ON RICKETS. M. ARMAND, Bol. Inst. internac. am. de protec. a la infancia **9:**264 (Jan.) 1936.

In Haiti, where rickets is rare, it is more often seen among the blacks than among the whites, and in the few cases that occur, it is very light. In Peru, Honduras and Uruguay it is also benign and generally disappears without leaving serious traces. The opinion prevails that the rickets observed in America is attenuated as compared with the more serious form observed in regions of Europe, and that this difference is due to the prophylactic influence of the sun, to breast feeding in first infancy and, later, to a system of feeding which affords abundant vitamins, though it is not correct in its form and essence. Congenital rickets does not occur. Rachitic disorders are contracted as a consequence of prolonged states of infection or of physiologic poverty.

Barbosa and Ygartúa replying to Armand's inquiry as to rickets in Brazil, consider syphilis an undeniable predisposing factor since it favors divers kinds of osseous dystrophy; Villarroel, Bolivia, attributes to syphilis a more important rôle; De Sierra, Bolivia, and Velasco, Ecuador, as well as Ordóñez Diaz, Honduras, consider the connection of the two diseases doubtful. Armand, Haiti, and Berro, Uruguay, point out the frequency of syphilis, almost 50 per cent of the population in Haiti and 10 per cent of that in Montevideo being affected, and the scarcity of rickets.

Generally, all the answers to Armand's inquiries coincide. Rickets is more common among the poorer classes; it is especially common in families that lack healthy dwelling places and sufficient food. This happens oftener in city tenements than in country huts, since in the country, whatever the dwelling-place, the child possesses the great resource of the sun, which shines the greater part of the year.

In Haiti, where, it has already been said, rickets is exceptional, spasmophilia is relatively frequent, particularly at the time of the first dental eruption. Armand has not found in spasmophilic subjects any clear signs of rickets, and he does not believe that these diseases have points of contact. Suares, Peru, finds that statistics disclose few cases of spasmophilia, but he proves that it exists in his country and that it has no connection with rickets. It seems that in Ecuador spasmophilia is very rare, as well as in Uruguay, where it is treated almost by the same methods as rickets, the therapeutic identity suggesting a similarity as to origin. The answer of Ordóñez Diaz from Honduras is a good résumé of the general causes which render rickets and spasmophilia nonfrequent in Spanish-American countries: "The scarcity of rickets among us is ascribed to the sun, which shines all the year round, to its intense luminous radiations, to open air life, to the extent of natural feeding still prevailing in the rural population, and to the abundance and consumption of fruit and vegetables rich in vitamins, such as oranges, bananas, pineapples, alligator pears, mangoes and tomatoes, which are given to children, according to age, in the form of juice or jam or other preparation.

In the answer from Uruguay, reference is made to Professor Morquio's constant commendation of the fundamental preventive influence of breast feeding. In Spanish-American countries the bibliography on rickets is limited. The same is true as to that on spasmophilia. The reason for this is no other than that the two diseases are rare on that continent.

LESLIE, Evanston, Ill.

DOSAGE OF VITAMIN C. O. F. F. NICOLA, Rev. med. latino-am. **31**:459 (Jan.) 1936.

A modified Tillman technic, also the iodine technic, was used to determine the units of vitamin C in lemon juice, orange juice and milk. It was found that orange juice and lemon juice kept at a temperature of 5 C. for thirty-one days maintained their vitamin C potency best, with the losses varying from 25 to 30 per cent. Fresh milk and pasteurized milk showed losses of from 34 to 38 per cent. A more rapid loss takes place in an alkaline or a neutral medium. Nicola favors a modification of the Clark method, in which the potential of oxidation is determined by colorimetric methods. DWYER, Kansas City, Mo.

A CORRECTION OF OUR PREVIOUS ARTICLE ON THE BLOOD-AQUEOUS BARRIER AND VITAMIN C. H. GOLDMANN AND W. BUSCHKE, Arch. f. Augenh. **109**:689, 1936.

In the previous article (*Arch. f. Augenh.* **109**:205, 1935) the cevitamic (ascorbic) acid content of the aqueous was determined in a series of rabbits for each of the two eyes and the values expressed as percentages. The mean error of these percentages was given in the previous article as ± 2.02. This was a mistake, as the correct value is ± 6.4. This mistake did not in any way affect the authors' conclusions.

Since a comparison of the value of the cevitamic acid in the aqueous of the untreated eye serves for a control in many of their experiments, they have examined the aqueous of the two eyes in thirteen more normal rabbits and compared the cevitamic acid contents. They report again that the mean difference in the cevitamic acid contents of the two normal eyes is quite small and that in any experiments wherein one eye is treated experimentally the cevitamic acid content of the fellow affords sufficient control. ADLER, New York. [ARCH. OPHTH.]

CIRCULATION OF BLOOD IN THE EYE AND VITAMIN C. W. BUSCHKE, Arch. f. Augenh. **109**:691, 1936.

The amount of cevitamic acid in the aqueous depends on the amount of the oxidized form of vitamin C in the blood. The vitamin C coming from the blood is reduced by the lens to cevitamic acid. This acid cannot get back into the blood stream because normally the blood-aqueous barrier is impermeable to its passage. If, however, this barrier is made more permeable, as by subconjunctival injections of salt solution, the amount of cevitamic acid in the aqueous falls, as numerous experiments have proved. Further, if the vitamin C in the blood is increased by feeding or by intravenous injection of a synthetic preparation of vitamin C, the cevitamic acid in the aqueous rises. This demonstrates the interesting fact that the lens not only can reduce ordinary amounts of vitamin C presented to it normally but has the capacity to take care of considerably larger quantities when these occur under experimental conditions.

Three factors are of importance in determining the quantity of cevitamic acid in the aqueous: (1) the size and blood flow of the uveal capillaries, (2) the permeability of the capillary walls for vitamin C and (3) their permeability for cevitamic acid.

The third factor was investigated in previous papers (Goldmann and Buschke: *Arch. f. Augenh.* **109**:314, 1935). The present communication deals with variations in the first two factors. These two factors cannot at present be separated. The authors therefore elected to use drugs which increase and decrease the size and the permeability of the capillaries of the uveal tract, i. e., acetylcholine and epinephrine.

In a series of rabbits a subconjunctival injection of epinephrine was given in one eye, followed at regular intervals by drops of epinephrine in the conjunctival sac. Then 100 mg. of a synthetic preparation of vitamin C was given intravenously to raise the vitamin C in the blood. The cevitamic acid content of each of

the eyes was then determined. As was to be expected, the control eye contained much more cevitamic acid than the eye treated with epinephrine. They ascribe this effect to diminution in the supply of vitamin C reaching the anterior chamber of the treated eye—hence, less for the lens to convert into cevitamic acid. They do not decide whether the widely dilated pupil in the eye treated with epinephrine was a factor in producing this effect or not.

In a second series of rabbits acetylcholine was injected subconjunctivally in one eye, and at varying periods the cevitamic acid contained in each anterior chamber was determined. In the majority of the experiments a considerable increase in the cevitamic acid content of the eye treated with acetylcholine was found, but the effect was not constant, and in one case a lower content of cevitamic acid was found. There seemed to be a more or less general agreement between the increase in cevitamic acid and the degree to which the capillaries retained their normal impermeability, for when the protein in the aqueous was found to be high after the use of acetylcholine (this was used as an index of increased permeability of the uveal capillaries) the cevitamic acid was not increased. Acetylcholine, according to these authors, must therefore have some peculiar effect on the eye which leads to an increase in cevitamic acid, besides its effect in increasing the permeability of the walls of the blood vessels. This action may be an increase in the blood flow through the uveal capillaries, which brings a greater amount of vitamin C into the anterior chamber. Here it is changed into cevitamic acid, and in this form it cannot escape from the anterior chamber back into the blood stream.

A discussion of technical points follows to proves that the effects the authors observed are in reality due to changes in the intra-ocular circulation.

ADLER, New York. [ARCH. OPHTH.]

THE AMOUNT OF VITAMIN C IN THE AQUEOUS OF NORMAL AND OF PATHOLOGIC EYES. A. GALA and J. MĚLKA, Arch. f. Augenh. **109**:726, 1936.

Gala and Mělka aspirated specimens of the aqueous from a series of patients and determined the cevitamic acid content for each. These specimens were divided into those (1) from normal eyes without any sign of inflammation, (2) from inflamed eyes and (3) from eyes containing senile cataracts. In the first group the ages ran from 13 to 60 years. In the second group the ages were from 16 to 65 years; in the third the youngest subject was 55 years old and the oldest 80 years old. Altogether, 165 eyes were examined. Since both eyes were examined at the same time, a good control was afforded.

They found that normal eyes have, on the average, around 4 mg. of cevitamic acid per hundred cubic centimeters of aqueous, while eyes the subject of inflammation have around 3 mg. Of the seventy-four instances of cataract of one eye, in seven the cevitamic acid content of the cataractous eye was the same as that of the control eye; in sixteen it was less, and in eleven it was greater than that of the control eye. In four cases in which one eye was aphakic and the other cataractous the cevitamic acid content of the aphakic eye was higher in two and lower in two than that of the fellow eye containing a cataract.

The assumption that the cevitamic acid in cataractous eyes is less than normal is not justified as a cardinal rule.

ADLER, New York. [ARCH. OPHTH.]

Hygiene; Growth and Nutrition; Public Health

A STUDY OF INFANT CARE IN A RURAL COMMUNITY. M. F. MURRAY and R. I. LYMAN, New York State J. Med. **36**:165 (Feb. 1) 1936.

At the Mary Imogene Bassett Hospital, Cooperstown, N. Y., the new-born infants have been in charge of a pediatrician since 1928. Mothers are given advice and instruction as to the care of their children before they leave the hospital. In a free follow-up clinic the children are seen at regular intervals up to the age of 2 years. Many of the patients are from rural districts. A marked reduction in both morbidity and mortality is shown.

AIKMAN, Rochester, N. Y.

RELATION BETWEEN HEALTH AND INTELLIGENCE IN SCHOOL CHILDREN. N. J. ENGLAND, J. Hyg. **36**:74 (Feb.) 1936.

Group tests were made to determine the intelligence of 959 children in rural elementary schools of England whose medical histories and environmental and physical status were well known. Relationships between serious or prolonged illnesses and the nutritional state as determined by weight and height were considered. Subgroups based on the types of previous illnesses, whether these occurred before school life or not, were formed, the data on the children in these subgroups were carefully tabulated, and the intelligence quotients of the different subgroups were listed.

In general, this rural group showed some excess of children whose intelligence was at the lower level. The incidence of common infectious diseases was little different from that in American children of a "gifted" group as noted by Terman.

The incidence of defects and of common infectious diseases was about the same in all directions according to levels of intelligence, the superior child being as much afflicted as the inferior. Neither the defects nor the diseases can have influenced the intellectual growth of these children. There was no association between intelligence and such conditions as bronchitis, pneumonia, infection of the tonsils, presence of adenoids, scarlet fever and visual defects.

The supposed correlation between the higher levels of intelligence and good nutrition may be erroneous. The association is rather between intelligence and physique. Both the lower physical development and the lower intelligence of certain children may be inherited.

JANNEY, Wauwatosa, Wis.

THE NUTRITION CLINIC FOR PRESCHOOL CHILDREN UNDER THE CHARGE OF THE URUGUAYAN ASSOCIATION FOR CHILD WELFARE. A. RODRÍGUEZ CASTRO, Bol. Inst. internac. am. de protec. a la infancia **9**:356 (Jan.) 1936.

It is necessary to encourage the establishment of institutions to take charge of the case of proschool children—such as dietetic clinics, kindergartens and sanitarian clinics—in order to apply and supervise prophylaxis at this stage of life, so rich in peculiar features and, at present, too much beset by hazard in its evolution.

The teaching of dietetics should tend toward the practical, the proponents paying attention to the needs in the given surroundings and looking for simple feasible solutions of the problems.

LESLIE, Evanston, Ill.

THE BUILDING OF "CRÈCHE" HOUSES. J. OBES POLLERI and R. GARCÍA BLIXEN, Bol. Inst. internac. am. de protec. a la infancia **9**:378 (Jan.) 1936.

Details of the construction of institutions for the care of infants are given.

LESLIE, Evanston, Ill.

OBLIGATORY AND RESTRICTED ARROGATION. P. F. CORAL LUZZI, Bol. Inst. internac. am. de protec. a la infancia **9**:425 (Jan.) 1936.

Coral Luzzi, with his original investigations and his rational innovations, advocates "obligatory and restricted arrogation" as the principal legal measure to protect helpless minors of illegitimate birth, attending to the fact that Uruguay and other states with similar legislation have excluded this matter from their codes without noticing that their provisions about adoption and guardianship will be powerless to attend to the claims of the unprotected beween 7 and 21 years of age, who wander along streets and roads seeking the protection and warmth of a home and die because of the indifference of selfish people, satiated with comfort and parsimonious in regard to charity.

LESLIE, Evanston, Ill.

CLASSIFICATION OF SCHOOL CHILDREN: HOW IT PROTECTS CHILDREN AND ADVANCES EDUCATION. L. HOURTICOU, Bol. Inst. internac. am. de protec. a la infancia **9**:438 (Jan.) 1936.

In the classification of school children attention should be paid to fundamental and not to accessory facts. The prime fundamental fact is not the quantity of knowledge a pupil may possess at a certain moment, considered as an absolute quantity, but its relation to such factors as his chronological age, his attendance at school, his state of health and his mental development. The classification should be such that it compels no pupil to make forced marches; however, this does not mean that there is an advantage in eliminating the stimulus to effort, which is salutary whenever it stimulates to action within normal limits. Nor should classification keep the child at a level inferior to that which he might reach without fatigue. All systems of rigid classification preventing the formation of groups that do not agree with the current groups should be avoided.

LESLIE, Evanston, Ill.

MUSICAL RECITALS FOR CHILDREN. ISMAELA NAVARRA, Bol. Inst. internac. am. de protec. a la infancia **9**:466 (Jan.) 1936.

Navarra acknowledges that musical recitals for children are an efficient means of complementing the work of esthetic musical education which singing and sol-fa classes and juvenile orchestras carry out in schools. She recommends to school authorities a methodical organization of these activities, and urges steps to facilitate the publication of works of musical literature in compliance with the programs to be executed in the course of the year.

LESLIE, Evanston, Ill.

Prematurity and Congenital Deformities

CONGENITAL FISSURATION OF THE STERNUM. E. KEWESCH, Röntgenpraxis **8**:100 (Feb.) 1936.

The sternum arises through the fusion of paired rudiments, which originate from the seven superior cartilaginous ribs. Failure of this to continue to completion is illustrated in the few cases of congenital partial defect of the sternum which have been described under the title "Fissura Sterni Congenita." In this paper Kewesch reports a case of congenital complete absence of the sternum: A 45 year old man, a Russian, presented a deep longitudinal depression in the midline of the thorax and abdomen as far as the umbilicus; the skin covering this area was scarred; the pulsations of the great vessels could be readily appreciated through the thin integument. The diagnosis of congenital fissuration of the sternum was confirmed by roentgenographic examination. The patient knew of no occurrence of similar lesions in other members of his family. He had no symptoms that were referable to the anomaly.

MCCUNE, New York.

APLASIA OF THE SACRUM. J. H. MÜLLER, Röntgenpraxis **8**:105 (Feb.) 1936.

The caudal portion of the vertebral column is a favorite site for congenital bony anomalies. These are frequently associated with severe developmental defects of the spinal cord and meninges which are incompatible with life. Such cases are of greater teratologic than clinical interest. About twenty cases of extensive congenital defect of the sacrum and coccyx have been reported in which the patients survived. To this number Müller adds the case of a 6 year old boy with congenital clubfoot and complete absence of the sacrum and coccyx. The child was incontinent of urine and feces and gave other evidence of disturbance of function of the lower segments of the spinal cord.

MCCUNE, New York.

A Morphological Study of Two Cases of Multiple Congenital Malformations of the Skeleton. K. Y. Ch'in, Chinese M. J., supp. 1, February 1936, p. 82.

Two cadavers, one that of a stillborn boy and the other that of a girl who died at the age of 10 days of purulent cerebrospinal meningitis from ruptured spina bifida, presented many congenital skeletal deformities. The study had special interest because some of the deformities were so rare as not to be found mentioned in the available literature. They were as follows: lumbar lateral mass; lateral flaring and ventral arching of the pedicles and laminae of the lumbar vertebrae; absence of alae of the sarcum; certain other deformities, such as lumbosacral dislocation and pelvic asymmetries. There were twenty-two deformities in the first child and twelve in the second. Ch'in describes each deformity in detail. He discusses the fact that the embryonic development of the human spine recapitulates the conditions found in primitive vertebrate animals, for in the early embryonic stage ribs are normally present on the twentieth (first lumbar), seventh (last cervical) and, occasionally, sixth vertebrae. During the stage of ontogenetic development the number of vertebrae bearing ribs becomes gradually reduced to the normal number for man. The interested reader is referred to the original article, which cannot be easily abstracted, because of the minute details.

Neff, Kansas City, Mo.

New-Born

Intra-Uterine and Neonatal Otitis: A Study of Seven Cases, Including a Case of Otitic Meningitis. F. A. Hemsath, Arch. Otolaryng. **23**:78 (Jan.) 1936.

Seven cases of otitis of various types in stillborn and new-born infants are reported by Hemsath. He states that the middle ear of the fetus at term may be the site of a foreign body and that an inflammatory reaction in the middle ear is probably due to the presence there of constituents of the amniotic fluid. Premature rupture of the amniotic sac accounts for the pus cells and bacteria in the middle ear of the new-born infant. Otitic meningitis with a secondary purulent labyrinthitis may cause death on the sixth day of life.

Greenwood, Chicago.

The Mechanics of Delivery, Especially as It Relates to Intracranial Hemorrhage. F. C. Irving, New England J. Med. **214**:635 (March 26) 1936.

During the past ten years at the Boston Lying-in Hospital 20,827 infants were delivered with an incidence of intracranial hemorrhage of 1 in 107. Neonatal deaths from intracranial hemorrhage have shown a steady drop since 1932, being 5.2 per thousand in that year, 3.8 in 1933 and 2.5 in 1934.

Intracranial hemorrhage may be due to trauma or to intra-uterine asphyxia; it may be a manifestation of hemorrhagic disease of the new-born. The chief cause is violent or unskilful operative delivery by means of forceps or in internal podalic version or breech presentation.

By far the most frequent source of fetal injury is delivery through an undilated cervix. The use of analgesic drugs in labor assuages the pains of labor and makes the attendant more willing to await the workings of nature. It is significant that the last three years, which have shown almost a 50 per cent drop in the neonatal stillbirth rate at the Boston Lying-in Hospital, cover the period of the routine use of hypnotic drugs.

The infant mortality rates for the different varieties of forceps operations have been: low forceps, 1.6 per cent; mid forceps, 7 per cent, and high forceps, 20 per cent.

From 1932 to 1934, inclusive, there were performed 53 versions and extractions in 8,617 deliveries, with the loss of 14 babies, a mortality of 26.4 per cent.

Gengenbach, Denver.

NEO-NATAL DERMATITIS. H. CARTER and H. A. OSBORN, Brit. M. J. **1**:465 (March 7) 1936.

A classification of dermatitis of various origins is made as follows: (1) simple infantile dermatitis (Jacquet); (2) syphilitic dermatitis; (3) erysipelas neonatorum; (4) bullous dermatitis due to mechanical or chemical irritants, and (5) pyodermatitis, which includes (*a*) folliculitis, (*b*) subepithelial dermatitis (pemphigus neonatorum) and (*c*) deep cutaneous abscesses.

The main body of the article, however, is concerned largely with pemphigus of the newly born. Prevention is most important, and the results in this respect have improved with careful supervision of the staff of nurses and other conditions. A summary of the study follows:

Pemphigus neonatorum is a contagious dermatitis, with a short incubation period of from one to five days. The lesion is situated under the epidermis and tends to spread centrifugally unless a reliable antiseptic is brought into immediate contact with the infecting organism. The contagiousness is due to the short period of incubation and the ease with which the primitive epidermis of the neonatal infant can be penetrated. As the source of the outbreak may be difficult to find, the disease tends to become epidemic. In a maternity unit where this disease is endemic, irregular waves occur in the graph of the cases; i. e., the number of cases increases with a rush of work in the department and drops in the "quiet" periods.

In the experience in Mill Road Infirmary the so-called Boston method of treatment did not prove to be of any value. The elimination of the source of infection is the ideal and only sound method of checking an outbreak.

The disappearance of cases of folliculitis at the same time as those of pemphigus neonatorum suggested that the two diseases are etiologically somewhat similar; histologic sections showed that the lesion of pemphigus neonatorum is subepithelial and therefore more dangerous.

It should be possible, by early diagnosis and intelligent and effective treatment, to lower and even practically abolish the mortality of the disease. The presence of pemphigus neonatorum in a maternity unit is an indication that there is a septic focus in, or associated with, that department, and the septic focus should be found and eradicated.

In the outbreak of pemphigus neonatorum at Mill Road Infirmary at least seventeen strains of Staphylococcus aureus and two of Staphylococcus citreus were found.

Pemphigus neonatorum should have only one phase, that of the small unbroken blister. If the treatment by silver nitrate described is followed, the subsequent phases should not occur. The authors differ entirely from Poole and Whittle (*Lancet* **1**:1323 [June 8] 1935), who stated that this disease is an acute infection, that recovery appears to depend on spontaneous development of immunity to the infecting organism and that it is doubtful if local treatment shortens the duration of the attack. They are convinced that this disease is not an acute infective fever but is merely a local subepithelial dermatitis and that local treatment can abort it. They protest strongly against the not only discouraging but totally erroneous dogma that patients who die have been doomed from the onset. The fatalities are due to late diagnosis and inefficient treatment. ROYSTER, University, Va.

THREE CASES OF INTRACRANIAL HEMORRHAGE OF THE NEW-BORN WITH RECOVERY. B. TASSOVATZ and S. TASSOVATZ, Bull. Soc. d'obst. et de gynéc. **25**:175 (Feb.) 1936.

Two of the infants concerned weighed at birth 3,450 and 3,350 Gm., respectively. The weight of the other infant is not stated. The first two were born by head presentation, the infants being delivered by forceps, placed high, and the third was born by breech presentation. All three infants showed alarming signs of intracranial hemorrhage. Lumbar taps showed grossly bloody fluid, the fluid clearing up after repeated punctures. Besides having a diagnostic value, the

punctures are of great therapeutic effect because of the decompressing action on the central nervous system and the diminution of the meningeal irritation by the extravašated blood. The infants left the hospital apparently well, but the ultimate prognosis must, of course, be guarded.

GLASER, Rochester, N. Y.

INFLUENCE OF CONGENITAL SYPHILIS ON THE OSSIFICATION OF THE LABYRINTHINE CAPSULE IN THE NEW-BORN. W. DÖDERLEIN, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **140**:229, 1936.

Döderlein describes histologic observations on the petrosas of newly born infants with congenital syphilis. Since the changes appeared only in the zone of enchondral ossification of the labyrinthine capsule, he reports only the observations on this region. In some cases the conditions were normal, but in others he observed an unusual acceleration of the ossification of this zone. In the latter group, the bone at many sites was even more compact than in the labyrinthine capsule of the adult. The author thinks that this acceleration in the ossification of the labyrinthine capsule is caused by syphilis. Thus it has been proved that congenital syphilis may cause not only retardation but acceleration of the ossification of the labyrinthine capsule. Whether these pathologic processes of ossification may later result in auditory disturbances cannot be decided as yet. The nervous elements of the cochlea were normal in the instances of pathologic ossification.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

PNEUMOTHORAX IN THE NEWLY BORN. J. VAN E. TENGBERGEN, Fortschr. a. d. Geb. d. Röntgenstrahlen **53**:240 (March) 1936.

Three cases are reported. In each instance the diagnosis was made by roentgenographic examination, which was carried out in one case because of cyanosis with moderate dyspnea and in the other two cases because of a weak, whining cry. The physical findings in these patients were equivocal. In one the mediastinum was somewhat displaced; in another the affected half of the chest was relatively more prominent than the opposite half, and the breath sounds were rather amphoric. In all three cases the air was resorbed spontaneously within a few days. The only common feature to which conjectural pathogenic import could be ascribed was the fact that in each instance the infant was born with the umbilical cord wrapped about its neck. Spontaneous pneumothorax is not particularly uncommon in adults and in older children nor is it excessively difficult to diagnose. It is generally regarded as rare in infants, and it readily escapes detection. The author lists eighteen previously reported cases in infants. The incomplete character of the data pertaining to these cases indicates clearly the need of more information concerning the condition. There is evidence to indicate that the condition is probably more common than has been generally suspected.

MCCUNE, New York.

Acute Contagious Diseases

IMMUNITY TO THE VIRUS OF MUMPS IN MONKEYS. C. D. JOHNSON and E. W. GOODPASTURE, Am. J. Hyg. **23**:329, 1936.

Evidence is presented that the only reliable experimental method of inducing active immunity to mumps in monkeys is that of causing a unilateral or bilateral clinical or subclinical specific parotitis by intraparotid inoculation. Some monkeys prove to be immune to intraparotid injection of the virus of mumps following the use of oral and nasal sprays of suspensions of the virus or after subcutaneous, intramuscular or intravenous injections of the virus; but these methods often fail to immunize. Attempts to confer passive immunity by injections of serum from persons immune to mumps have, with rare exceptions, failed. There are indications

that the virus of mumps may infect the nerve tissue of monkeys after intracerebral injection. Immunity to infection from intraparotid injection of the virus has followed quite regularly a single intracerebral injection.

FROM THE AUTHORS' SUMMARY. [ARCH. PATH.]

SUSCEPTIBILITY OF THE GUINEA PIG FETUS TO VACCINIA. J. STRITAR and N. P. HUDSON, Am. J. Path. **12**:165 (March) 1936.

The virus of vaccinia has been successfully propagated in the fetal guinea-pig. The virus induced typical lesions in various organs and tissues. The same strain of virus caused only the slightest reaction in the new-born or young animal. These results indicate a markedly greater susceptibility of fetal tissues for the infectious agent. The cultivation by other workers of certain viruses in embryonic tissues, though adults of the same species were not reactive, points to the same phenomenon. The mechanism of this comparative effect is not yet clear, although the general immaturity and rapidity of cell growth in the fetus are suggested as possible factors. Lesions were found irregularly distributed in the principal organs, including the skin, and were most common in the lungs and kidneys. Of all the fetal tissues, the kidney yielded the virus most constantly and with the highest titer, usually 1 : 10,000. The virus was passed through a series of fetuses and was not appreciably modified in its cutaneous activity in the rabbit or in its failure to induce effects in the new-born or young guinea-pig.

MOORE, New York. [FROM THE AUTHORS' SUMMARY.]

NATURAL IMMUNIZATION TO DIPHTHERIA IN AN INSTITUTION. C. C. YOUNG, G. D. CUMMINGS and M. E. WILSON, Am. J. Pub. Health **25**:43 (Jan.) 1935.

Studies were made of 389 patients in an institution by means of the Schick test, the throat swab and the titration of blood antitoxin at intervals of three, six and nine months for evidence of herd immunization. The number of positive reactions to the Schick test was reduced 35 per cent in the untreated group, 50 per cent in the (substandard preparation) toxoid group and 89 per cent in the toxin-antitoxin group. Negative reactions were found in 11.3 per cent of the patients who had 0.01 unit or less of antitoxin per cubic centimeter of blood; these persons responded rapidly to diphtheria antigen. The Schick test often causes an increase in the antitoxin in the blood. Diphtheria has not been endemic in the institution since 1920, so the foregoing results possibly indicate that herd immunization was taking place continuously through the medium of organisms of low virulence which had lost their ability to cause clinical diphtheria.

McBRYDE, Durham, N. C.

ACTIVE IMMUNIZATION AGAINST POLIOMYELITIS. M. BRODIE, Am. J. Pub. Health **25**:54 (Jan.) 1935.

Brodie reviews the work on active immunization against poliomyelitis in which he used a suspension of virus inactivated by solution of formaldehyde U. S. P. An appreciable antibody response occurred in monkeys and human beings who were given the vaccine. Immunity was present in monkeys three months after immunization with the formaldehydized virus.

McBRYDE, Durham, N. C.

SIGNIFICANCE OF BACTERIOLOGIC METHODS IN THE DIAGNOSIS AND CONTROL OF WHOOPING COUGH. P. KENDRICK and G. ELDERING, Am. J. Pub. Health **25**: 147 (Feb.) 1935.

The authors report the use of cough plates as a routine in diagnosing pertussis and in determining which patients to isolate and which to release. In 332 cases of pertussis 78 per cent of the plates were positive in the first week, 64 per cent in the second, and 62, 32, 15 and 3 per cent in the third to sixth weeks, respectively. They believe bacteriologic release is as important in pertussis as in certain other diseases in which it is practiced. The criteria for the selection of cultures and the technic of preparing Bacillus pertussis vaccines are outlined.

McBRYDE, Durham, N. C.

DIPHTHERIA IMMUNIZATION BY ONE INJECTION. V. K. VOLK, Am. J. Pub. Health **25**:430 (April) 1935.

Volk finds that the injection of alum-precipitated toxoid (one dose) is superior to other methods. He believes the duration of immunity following the injection of alum-precipitated toxoid needs careful investigation.

McBRYDE, Durham, N. C.

REACTION OF FAMILIAL CONTACTS TO SCARLET FEVER INFECTION. J. E. GORDON, G. R. BADGER, G. R. DARLING and S. S. SCHOOTEN, Am. J. Pub. Health **25**:531 (May) 1935.

An urban population of 5,352 persons (1,097 families) had scarlet fever. Secondary attacks occurred at the rate of 7.3 per cent. Endemic scarlet fever may first appear in the home as a simple respiratory infection in an immune or partially immune person. Failure to recognize the first case of scarlet fever increases the rate at which secondary cases occur; 31.6 per cent of secondary cases were due to this failure. Except in familial cases, the disease is largely transmitted by carriers. Infections of the upper respiratory tract are quite frequent among persons recently exposed, and many of these infections are associated with developing immunity to scarlet fever if one may judge by the Dick test; immunity developed in 14.8 per cent of those in contact with patients who had the disease and was more frequent in those who had hemolytic streptococci in the nose and throat.

There is need for earlier recognition of cases and isolation of the patients. A shorter period of isolation is equally effective, as secondary cases in families appear after a short interval. It is important to isolate patients briefly, especially those in a family who have been in contact with scarlet fever and who have infections of the upper respiratory tract.

McBRYDE, Durham, N. C.

DIPHTHERIA STUDIES: II. USE OF INTRADERMAL INJECTIONS OF TOXIN-TOXOID MIXTURES IN DIPHTHERIA IMMUNIZATION. W. E. BUNNEY, Am. J. Pub. Health **25**:623 (May) 1935.

A toxin-toxoid mixture containing 0.5 Lf per tenth cubic centimeter was given intradermally to ascertain if it could be used for the dual purpose of immunizing and testing for immunity to diphtheria. This procedure increased the percentage of children immunized when it was followed by any of the usual methods of immunization. The antitoxin content of the blood in adults increased after intradermal use of the toxin-toxoid mixture.

McBRYDE, Durham, N. C.

FREQUENCY OF IMMUNIZING PROCEDURES OF VARIOUS KINDS IN NINE THOUSAND FAMILIES OBSERVED FOR TWELVE MONTHS, 1928-1931. S. D. COLLINS, Am. J. Pub. Health **25**:1221 (Nov.) 1935.

The 8,758 white families (including 39,185 persons) surveyed lived in 130 localities in 18 states and represented all geographic sections of the United States. Vaccinations against smallpox reached a maximum of 66 per cent by 16 years. Between 60 and 76 per cent of the adults had been vaccinated against smallpox at some time in their lives. Immunization against diphtheria reached a maximum of 43 per cent at 9 years of age, and at the present rate about one half of the population will eventually be immunized.

Immunizations against typhoid reach a maximum of 10 per cent at 17 years of age and 12 per cent between 30 and 45 years of age. This procedure is more common in the South than in other sections of the country.

McBRYDE, Durham, N. C.

STUDIES OF HEMOLYTIC STREPTOCOCCAL INFECTION: I. FACTORS INFLUENCING THE OUTCOME OF ERYSIPELAS. C. S. KEEFER and W. W. SPINK, J. Clin. Investigation **15**:17 (Jan.) 1936.

The general mortality from erysipelas determined in a survey of the records of 1,400 cases at the Boston City Hospital was 16.4 ± 3.6 per cent. In this group the most important general factors influencing the mortality were age, debilitating diseases and bacteremia. Mortality was highest in the patients under 2 and over 70 years of age. Erysipelas had the same seasonal incidence as other streptococcic infections and frequently began in an acute infection of the nasal passages with hemolytic streptococci.

GUEST, Cincinnati.

EXPERIMENTS ON ACTIVE IMMUNIZATION AGAINST EXPERIMENTAL POLIOMYELITIS. P. K. OLITSKY and H. R. COX, J. Exper. Med. **63**:109 (Jan.) 1936.

Olitsky and Cox investigated the possibility of active immunization of monkeys (Macacus rhesus) against poliomyelitis by means of chemically treated virus. They employed tannin-precipitated virus and virus treated with sodium ricinoleate and with solution of formaldehyde U. S. P. The experiments showed plainly that such chemical treatment did not act to attenuate the virus.

The results can be summarized by stating that if the immunizing agent contains a sufficient amount of virus, the danger arises that the animal will be infected with the virus. Under the experimental conditions employed, these preparations, although active virus was present in them, failed to immunize the inoculated animals regularly. Antiviral bodies were produced in the serums by the methods described, but the animals in which these antibodies were present did not show resistance in the ordinary tests for active immunity.

A study of the records of attempts at immunizing monkeys against poliomyelitis during the past twenty-five years reveals that the active virus is not itself a potent antigen, as are some other viruses; uniform protection is rarely brought about through its use.

KNICKERBOCKER, Dallas, Texas.

RESPIRATORY VERSUS GASTRO-INTESTINAL INFECTION IN POLIOMYELITIS. S. FLEXNER, J. Exper. Med. **63**:209 (Feb.) 1936.

The debated problem of the gastro-intestinal versus the respiratory mode of infection in poliomyelitis has been restudied by several investigators recently, with conflicting results. Kling and Levaditi in Europe carried out experiments from 1929 to 1933, which led them to the conclusion that the digestive tract affords the virus of the disease a ready entrance into the body. They believe that a substitution of Macacus cynomolgus for Macacus rhesus as the species of choice for the tests supports this point of view. Toomey in the United States has arrived at a similar conclusion, not by employing monkeys of a particular species for experiments, but by using drastic measures of inoculation which insure that the virus makes contact with the unmyelinated nerve fibers embedded in the intestinal wall.

Flexner repeated the tests of Kling and Levaditi but failed to confirm their conclusion. He simply states: "On the basis of the experiments reported in this paper we can reaffirm the conclusion previously arrived at by ourselves, and confirmed independently by investigators in Europe and America, namely that the only established portal of entry of the virus of poliomyelitis into the central nervous system of man is the nasal membrane, and especially the olfactory nervous areas in that membrane."

KNICKERBOCKER, Dallas, Texas.

TREATMENT OF SCARLET FEVER AND DIPHTHERIA. C. WESSELHOEFT, M. Clin. North America **19**:1389 (March) 1936.

The treatment of scarlet fever resolves itself primarily into a consideration of serum therapy. When serum is used early in the disease, the toxic symptoms usually rapidly disappear. The frequent occurrence of serum sickness and the

occasional development of the Arthus reaction render the routine use of serum of doubtful advantage. The use of convalescent serum, when obtainable, in severe toxic scarlet fever is growing in favor. Serum therapy has no appreciable effect on complications after these have appeared. Its value as a measure prophylactic against complications is in dispute.

The prevalence of a malignant type of diphtheria in Europe has excited interest in this disease anew and has led many observers to doubt the value of antitoxin therapy. This position, however, does not seem to be well taken when it is recalled that serum therapy in diphtheria is essentially protective. It does not dissolve the diphtheritic membrane or destroy the bacilli. It does neutralize the toxin. In the malignant form of the disease, some as yet unknown factor lowers individual resistance to a virulent strain of organisms endowed with increased penetrating and increased toxin-forming properties. Against this form antitoxin is ineffective because it cannot protect against the overwhelming infection; reliance can be placed only on the earliest possible use of serum and repetition of the injection, with moderate dosage, at frequent intervals. EUGENE SMITH, Ogden, Utah.

SCARLET FEVER IMMUNITY (PRODUCTION AND MAINTENANCE): A STUDY OF COMPARATIVE VALUES OF RAW AND MODIFIED STREPTOCOCCAL TOXINS. R. J. REID, New York State J. Med. **36**:403 (March 15) 1936.

Dick tests were made on 3,000 inmates of a state institution; 200 reacted positively. Studies were made on these persons to determine the relative value of raw and modified toxins. It was found that raw toxin modified by oxygenation still retained its immunity-producing power. While raw toxin gave the greatest number of immunes, the results obtained with modified toxin lasted longer. The local and general reactions were more marked with modified toxin.

AIKMAN, Rochester, N. Y.

FIVE HUNDRED CASES OF SCARLET FEVER CAUSED BY USE OF RAW MILK FROM INFECTED COW. Pub. Health Rep. **52**:113 (Jan. 22) 1937.

Five hundred cases of scarlet fever in Oswego, N. Y., were found to be due to the use of raw milk from a single infected cow in a dairy herd. As a result of this the city has passed an ordinance requiring pasteurization of all milk sold there.

SANFORD, Chicago.

SUPPLY OF MEASLES ANTISERUM. G. C. WILLIAMS, Brit. M. J. **1**:471 (March 7) 1936.

This article is a description of the methods of the board of health for keeping on hand and supplying on demand convalescent serum from patients who have had measles within two months and also adult serum from patients who have had measles within ten years.

ROYSTER, University, Va.

A YAWS CAMPAIGN AND AN EPIDEMIC OF POLIOMYELITIS IN WESTERN SAMOA. S. M. LAMBERT, J. Trop. Med. **39**:41 (Feb. 15) 1936.

Lambert describes the method of the wholesale treatment of yaws in Samoa from 1923 to 1926. Twenty-five thousand patients received three injections each, with the result that primary and secondary yaws almost disappeared and only a few children under the age of 4 years required treatment for the disease.

From 1926 to 1931 treatment was almost abandoned, and in 1932 primary and secondary lesions were again abundant. In that year injections of neoarsphenamine were again given, but in some districts visited an epidemic of poliomyelitis followed. In 1933 injections were again given to many thousands of patients, and the lesions of yaws were found to be much improved over the preceding year.

Analysis of the results of Kahn tests made on school children showed that the incidence of negative reactions resulting from treatment with the arsenicals varied from 80 to 16 per cent.

Lambert concludes that the amount of treatment which could be given was not highly effective in sterilizing the blood of patients with yaws.

JAMIESON, Detroit. [ARCH. DERMAT. & SYPH.]

TREATMENT OF MALIGNANT AND SEVERE DIPHTHERIA WITH LARGE DOSES OF STRYCHNINE. G. PAISSEAU, J. BRAILLON and C. VAILLE, Bull. Soc. de pédiat. de Paris **33**:101 (Jan.) 1935.

During a period of six months 108 cases of diphtheria were observed. Twenty-three of these were of the malignant or grave type. In the latter group, large amounts of strychnine, as much as 1 mg. per kilogram of body weight per day in equal divided doses, were administered. The initial dose should be small, and subsequent doses should be rapidly increased; the daily dose should be divided into six or eight equal amounts and these injected regularly every three or every four hours. The patient should be watched carefully throughout the treatment, but if no untoward effects are observed within fifteen minutes after an injection, none are to be expected. With a daily dose of 0.5 mg. per kilogram of body weight no reaction was observed, but with larger doses toxic manifestations, such as muscular contractures, were noted. The drug was used as long as the condition seemed critical, usually for about fifty days. It is concluded that this treatment should be reserved for severe and malignant diphtheria, and should be given after the administration of antidiphtheritic serum; in such cases it may improve the immediate as well as the ultimate prognosis.

BENJAMIN, Montreal, Canada

INFECTIOUS ERYTHEMA (DISCUSSION CONCERNING ERUPTIVE FEVER). H. GRENET, P. ISAAC-GEORGES and G. BRÉHIER, Bull. Soc. de pédiat. de Paris **33**:106 (Jan.) 1935.

A girl 9½ years old and a boy 13 years old were admitted to the hospital within a few weeks, with similar conditions. Each had a benign febrile illness accompanied by a papulo-erythematous skin rash. Blood cultures were negative. The Weil-Felix reaction was negative. Brill's disease was therefore eliminated. There was no contact with dogs, which are the usual carriers of tics responsible for eruptive fever. The cases reported resembled the cases of eruptive fever previously described, but the condition could not be diagnosed definitely as such.

BENJAMIN, Montreal, Canada.

RENAL FUNCTION IN SCARLET FEVER. J. BAYART and L. ELAUT, Compt. rend. Soc. de biol. **118**:387, 1935.

Thirty cases were observed in children aged from 6 to 15: four without scarlet fever; twenty-eight with scarlet fever. Eighteen of the children who had scarlet fever were without hypertension or albuminuria; seven had hypertension but no albuminuria, in one of whom glomerulonephritis developed in the third week.

The arterial hypertension occurring in the third week of the disease varied and was not commensurate with the changes in the renal function. The phenolsulfonphthalein test showed decreased excretion in the patient who also had nephritis. In others in which albuminuria was present the water test (1,000 cc. daily) showed changes in urinary concentration even to a horizontal curve in patients having more disturbances. No observations are recorded relative to the changes in convalescence, i. e., as to the recovery of renal function.

WAHL, Cleveland.

RELATION BETWEEN ACETONURIA AND HEPATIC INSUFFICIENCY IN SCARLET FEVER. A. SLĂTINEANU, I. BĂLTEANU, M. SIBI, E. BUTESCU and Z. PARASCHIVESCU, Compt. rend. Soc. de biol. **118**:1592, 1935.

In fifty patients with scarlet fever, the following determinations were made: In twenty-seven the disease occurred with acetonuria, and in twenty-three, without. Bilirubinemia increased in 18 per cent of the patients with acetonuria and in 19 per cent of those without acetonuria; urobilinuria, in 85 per cent of those with and 90 per cent of those without acetonuria; glycosuria, in 51 per cent with and 70 per cent without acetonuria. The salicylate test for antitoxic function of the liver was positive in 85 per cent with and 81 per cent without acetonuria. The ammoniacal coefficient was elevated in 80 per cent with and 43 per cent without acetonuria. Creatinine increased in 30 per cent with and 25 per cent without acetonuria. Urea was practically unchanged. The alkali reserve diminished in 86 per cent with and 40 per cent without acetonuria. It is therefore noted that the hepatic function is at least less efficient in the patients who show acetonuria. WAHL, Cleveland.

TREATMENT OF HEINE-MEDIN DISEASE BY VACCINATION AGAINST RABIES. D. VON MÓRITZ, Arch. f. Kinderh. **105**:239 (July 16) 1935.

Treatment of Heine-Medin disease (anterior poliomyelitis) by antirabies vaccination, as first recommended by Barla-Szabó, was used in five cases. No therapeutic results were observed. CRANE, Chicago.

GANGRENE IN SCARLET FEVER AND DIPHTHERIA. K. BLUMBERGER, Arch. f. Kinderh. **107**:154, 1936.

Various underlying conditions come into question in consideration of gangrene in scarlet fever and diphtheria: embolism, thrombosis, toxic injuries of capillaries (fragility of capillaries), proliferative endothelial processes and injuries of the skin itself.

In scarlet fever there is a favorite time for the appearance of gangrene and in diphtheria a favorite place for its development.

The author's own observations include (1) gangrene of the lower part of the left leg from emboli in the arteria poplitea and gangrene in two areas on the right leg of a patient with scarlet fever and (2) several gangrenous lesions of the skin of both legs in a patient with diphtheria. CRANE, Chicago.

ROENTGEN RADIATION IN THE TREATMENT OF ERYSIPELAS IN INFANCY AND CHILDHOOD. P. SONNAUER, Arch. f. Kinderh. **107**:225, 1936.

Excellent results were obtained from roentgen therapy. CRANE, Chicago.

CONSTITUTIONAL DISPOSITION TO DIPHTHERIA. H. SECKEL, Jahrb. f. Kinderh. **145**:117 (Sept.) 1935.

Two groups of children with diphtheria were studied from the point of view of a hereditary innate disposition to contract severe diphtheria. One of the groups consisted of 141 children with toxic diphtheria, 49 of whom died. The other consisted of 159 children with severe diphtheria accompanied by croup, 30 of whom died. From a consideration of case histories together with family histories Seckel concludes that there is a familial predisposition to have severe diphtheria. The exudative diathesis is reported present in approximately 60 per cent of these patients. Status lymphaticus was noted in 7 of the 70 children who came to autopsy. Most of these came to sudden early death. Rather frequently cerebral anomalies were found associated with physieal deformities, especially in the group with toxic diphtheria; in part this observation is a result of the occurrence of an epidemic of diphtheria in an asylum for the deaf and dumb. As a consequence, the proportion of biologically inferior children in this series is unusually high, 5 per cent.

LANDAU, Hannibal, Mo.

PERMANENT LESIONS IN THE HEART FOLLOWING DIPHTHERIA. H. SCHUPPLER, Jahrb. f. Kinderh. **145**:135 (Sept.) 1935.

Schuppler feels that the paucity of permanent changes in the heart following diphtheria may be explained by the fact that lesions near the conduction system are most likely to cause death before there is time for cicatrization, while small lesions situated elsewhere in the myocardium heal without causing any noteworthy functional disturbance. Examples of both types are given.

More frequent use of the electrocardiogram in following these cases is urged.

[G. W. Parade and U. Petersen (*Jahrb. f. Kinderh.* **145**:22 [July] 1935) found that slight permanent changes may occur in the QRS complex as a result of diphtheria.—Abstractor.]

LANDAU, Hannibal, Mo.

HISTOPATHOLOGY OF SCARLATINAL MASTOIDITIS. M. A. POSNJAK and P. J. GEHRKE, Monatschr. f. Ohrenh. **69**:1062, 1935.

Posnjak and Gehrke emphasize that not only the type and course of scarlatina itself vary but also its otic complications. They think that this variance is chiefly due to reduction in the reactive capacity of the organism. In accordance with this, they differentiate between a toxoreactive and a toxo-anergic form. In the first instance the otitis differs only slightly from the ordinary form, whereas in the second the depth of the usually necrotizing process and its extension, rapidity and particularly its character are as a rule surprising. Thus it seems likely that the otitis that accompanies the milder forms of scarlet fever differs in the histologic aspects from the otitis that accompanies the septic forms. The authors studied nineteen cases of scarlatinal mastoiditis, in six of which the scarlet fever took a mild course and in thirteen a severe course. Of the latter, in one case it was of toxic, in the other twelve of septic, character. In studying the histologic aspects of the mastoiditis that accompanies the milder forms of scarlet fever, the authors were surprised by the intensity of the involvement of the bone and of the cellular contents. In all of the examined cases they noted early destruction of the epithelial elements and of the mucous membrane. In the bone, there were no signs of apposition, only signs of intense resorption. In septic mastoiditis the necrotic processes predominated. They involved not only the cell structure but also the bone substance of the mastoid process. Only in the cases in which the infection was perhaps slightly less virulent did there develop beside the necrotic processes also signs of reactive inflammation. The authors think that in the necrotic forms of mastoiditis the entire pneumatic system should be removed in the course of the operation.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

ENCEPHALITIS COMPLICATING VARICELLA. H. ZISCHINSKY, München. med. Wchnschr. **82**:1908 (Nov. 29) 1935.

A 7 year old boy was convalescing from moderately severe scarlet fever. On the thirty-eighth day of his illness varicella developed, which was complicated four days later by encephalitis. The signs of encephalitis disappeared after three weeks, and the patient made a complete recovery.

BRAHDY, Mount Vernon, N. Y.

EFFECT OF RETICULO-ENDOTHELIAL BLOCKADE ON VACCINATION. O. MÜNDEL and S. ZURUKZOGLU, Ztschr. f. Immunitätsforsch. u. exper. Therap. **86**:87, 1935.

Among the different attempts to explain the origin of postvaccinal encephalitis, that of van Bogaert was based on the genetic relation between the skin and the central nervous system. When the former fails in its function, the blood-cerebrospinal fluid barrier breaks down, and invasion of the central nervous system results. H. Schmid reported experimental confirmation of this hypothesis by blocking the reticulo-endothelial system of the rabbit with acriflavine hydrochloride and finding after subsequent vaccination a very insignificant cutaneous reaction and the development of encephalitis with positive anatomic findings. Mündel and Zurukzoglu

repeated the experiments of Schmid but failed to observe encephalitis. They did note a more rapid development of the cutaneous lesion, its lessened intensity and quicker disappearance as well as an earlier appearance and a lower titer of virucidal substances in the blood as compared with the findings in normal controls.

DAVIDSOHN, Chicago. [ARCH. PATH.]

CONCENTRATION OF DIPHTHERIA ANTITOXIN. A. ABIKO, J. Orient. Med. **29**:334 (March) 1936.

Abiko found that through the use of aluminum and potassium sulfate and of cadmium chloride albumin could be removed from diphtheria antitoxin without lowering the potency of the antitoxin.

LESLIE, Evanston, Ill.

ETIOLOGY OF POSTVACCINAL ENCEPHALITIS. LORENTZ HEERUP, Hospitalstid **79**: 169 (Feb. 18) 1936.

Twelve days after two sisters aged 4 and 7 years had been vaccinated against smallpox they fell ill with fever, somnolence, headache and rigidity of the neck. Both cerebrospinal fluids were clear but contained from 150 to 180 mononuclear cells. The younger sister was discharged healthy twelve days after her admission to the hospital; the older sister died on the second day of illness. At the postmortem examination there were found: infectious hyperplasia of the tonsils, lymphatic glands, thymus and spleen; diffuse nonsuppurative inflammation of the cereberum and medulla oblongata; degeneration of the liver and kidneys, and marked hyperemia of the lungs. Aseptic bacteriologic examination disclosed an infection of the tonsils and lungs with Staphylococcus aureus-haemolyticus, whereas other organs were found sterile. Herrup is of the opinion that the vaccinal virus blocked the reticulo-endothelial system, and in this manner lowered the resistance of the organism to the staphylococcic infection, the toxins of which were the cause of the encephalitis.

WALLGREN, Gothenburg, Sweden.

POLIOMYELITIS WITH RESPIRATORY FAILURE TREATED WITH THE RESPIRATOR. ROLF BERGMAN, Hygiea **98**:179 (March 31) 1936.

Bergman has treated fifteen patients with paralysis of the respiratory muscles from poliomyelitis in a respirator (a modified type of Drinker's respirator). In every case the sensation of suffocation was relieved and the oxygenation of the blood improved. Only six of the patients survived, however, and two of the remaining nine patients died of pneumonia and seven of circulatory failure.

WALLGREN, Gothenburg, Sweden.

Acute Infectious Diseases

PERICARDIAL LESIONS IN RHEUMATIC FEVER. C. K. FRIEDBERG and L. GROSS, Am. J. Path. **12**:183 (March) 1936.

Eighty-seven cases of rheumatic fever were examined for gross and microscopic lesions of the pericardium. The cases were divided into five groups: (1) active disease, with death in the first attack; (2) active disease, with death in the second recurrence; (3) active disease, with death in the third or a subsequent recurrence; (4) active disease, with cardiac failure but no clinical evidence of activity, and (5) inactive disease. Typically, group 1 showed acute inflammation and degeneration of collagen; groups 2 and 3, a thickening of the pericardial membranes and almost universal adhesions, and groups 4 and 5, mild lesions, such as round cell infiltration and increased vascularization. A change of some type was found in the pericardium in almost 100 per cent of the cases.

MOORE, New York.

THE USE OF HISTAMINE IN RHEUMATISM. F. S. MACKENNA, Brit. J. Phys. Med. **10**:187 (March) 1936.

Mackenna believes that therapeutic ionization of histamine gives better results in rheumatism than injection of the drug. He presents a technic and discusses the complications and results.

HARTMAN, Cleveland.

ABORTUS FEVER. D. PATERSON, Proc. Roy. Soc. Med. **29**:502 (March) 1936.

Abortus fever in a girl 4 years and 8 months old is reported.

WILLIAMSON, New Orleans.

MALARIA AND RELAPSING FEVER FOLLOWING BLOOD TRANSFUSION. C. W. WANG and C. U. LEE, Chinese M. J. **50**:241 (March) 1936.

From the department of medicine of Peiping Union Medical College, Wang and Lee report 54 cases of benign tertian malaria and 6 cases of relapsing fever following transfusions of blood in 3,700 persons of various ages. Some of these contracted malaria from a single transfusion, namely, an infant of 1½ months, an infant of 4 months, a child of 2 years and a child of 6 years. A pregnant mother who received a transfusion contracted relapsing fever therefrom and infected her premature infant, who died of the disease.

NEFF, Kansas City, Mo.

OCCURRENCE OF WEIL'S DISEASE IN SWEDEN. B. MALMGREN, Nord. med. tidskr. **11**:379 (March 7) 1936.

The first observation of Weil's disease in Sweden was made in 1923, the next ten years later, and since then 20 new cases have been reported, 7 of which were fatal. Malmgren has made 960 serologic examinations for agglutinins against Spirochaeta icterohaemorrhagiae on blood from patients suffering from symptoms that indicated that a Gruber-Widal test should be made. He found in 7 of the blood specimens a reaction positive for Weil's disease. In only 2 of these cases had there been jaundice; in the remaining 5 cases no clinical symptoms had been noted that suggested Weil's disease. Of 160 rats from different parts of Sweden, icterohaemorrhagiae was demonstrable in 52 per cent.

WALLGREN, Gothenburg, Sweden.

Chronic Infectious Diseases

CONGENITAL SYPHILIS IN CHILDREN: RESULTS OF TREATMENT IN FIVE HUNDRED AND TWENTY-ONE PATIENTS. F. R. SMITH JR., Am. J. Syph., Gonor. & Ven. Dis. **20**:45 (Jan.) 1936.

This article is part 2 of a series of articles on this subject. It may be summed up as follows:

A study of certain factors in 370 children with late congenital syphilis is presented, with the end-results of treatment of 242, who were followed for a period of from two to fifteen years. These results are compared with those obtained in a study of an older group observed in the clinic for syphilis in adults, previously reported.

The distribution of cases according to race and sex was similar to that in the group of children with early congenital syphilis.

Presumably as a result of treatment at an earlier age, fewer relapses occurred in the group studied than in patients seen after they had reached puberty.

The age at which relapses occurred was not different from that in untreated patients, leading to the conclusion that, though treatment may prevent relapses, it does not change the age of their appearance.

Interstitial keratitis was the most common form of relapse. Second to it was syphilis of the central nervous system. No instances of eighth nerve deafness were found in the group of young patients.

In no instances except those of involvement of the central nervous system was death attributable directly to syphilis.

The incidence of relapses decreased with increase in the amount of treatment; it was not quite twice as high in patients whose serum reactions were Wassermann-fast as in those whose reactions were reversed by treatment. It was found that a relapse may occur in a patient with a negative Wassermann reaction.

Patients with syphilis of the central nervous system did not respond well to treatment, and some of them continued to deteriorate in spite of it and in spite of negative Wassermann reactions of both the blood and the spinal fluid.

Wassermann-fastness was found in 71 per cent of the patients. It was present in 39.6 per cent of the patients whose treatment began when they were between the ages of 2 and 4; it was present in rapidly increasing percentages, up to 84 per cent, in those in whom treatment was not begun until they were from 11 to 15 years of age.

All syphilitic lesions except those resulting from involvement of the central nervous system healed readily under proper treatment. Only in certain cases of interstitial keratitis was it necessary to give more than two courses to obliterate such lesions.

ROYSTER, University, Va.

HUMAN TUBERCULOSIS OF BOVINE ORIGIN IN STAFFORDSHIRE. A. S. GRIFFITH and J. MENTON, Brit. M. J. **1**:524 (March 4) 1936.

This article represents a survey of tuberculosis in general in one locality. There is particular reference to nonpulmonary involvement—involvement of cervical glands, meningitis and tuberculosis of bones and joints. Human and bovine infection are compared. Special reference is made to tuberculous infection of the bovine type in human beings.

ROYSTER, University, Va.

THE PRACTICAL APPLICATION OF B.C.G. VACCINE IN THE PROPHYLAXIS OF TUBERCULOUS INFECTION IN CHILDREN. E. RIST, Edinburgh M. J. **43**:172 (March) 1936.

Rist read this paper at a meeting of the Tuberculosis Society of Scotland on June 25, 1935. He reviews briefly the beginning of the experiments in 1908 and 1913 on animals with use of the new nonvirulent strain of vaccine devised by Calmette and Guérin (BCG). He then discusses the application of this method of immunization to human beings in whom prevention must precede infection. Only children having a negative Pirquet test are suitable for inoculation with BCG.

Calmette has given the vaccine by mouth as an alternative to injecting it subcutaneously, the latter meeting with some objections because of the occasional formation of an abscess. In France alone, from July 1924 till March 1932 nearly one-half million infants received BCG by mouth. Other countries have used the vaccine to a limited extent. There is practically universal agreement that in infants BCG is innocuous. The difficulty has been to determine how universal the protection is among vaccinated children. There has been considerable criticism as to the methods used in statistical computation as regards the influence on the death rate in tuberculosis. Oral administration does not regularly immunize all the children, so that it must be regarded as an uncertain method of vaccination.

Rist then devotes the remainder of his article to the methods used by Arvid Wallgren in Sweden. Wallgren has made two very useful contributions: 1. He has developed the intracutaneous vaccination with BCG preferably with a dose of 0.05 mg. Following this the Pirquet test is usually positive in about seven weeks, but further injections may be necessary before the reaction will become positive. 2. He has advised that the children may need to be isolated in an institution or private home during the period of the vaccination so that there will be no possibility of becoming infected. There were 230 children who became allergic from the vaccination with BCG and were then exposed to tuberculous infection in

their homes. These children were examined clinically and by roentgenogram at least once a year, and only one, a boy living with a father and brother suffering from open pulmonary tuberculosis, had any tuberculous symptoms, and his symptoms were mild, the lesions soon healing entirely. The fate of all the children in Wallgren's material is known, and this concludes a perfect experiment. Vaccination with BCG is able to prevent virulent infection in previously uninfected children, but the immunity conferred is probably neither absolute nor lasting. If children are to be exposed to virulent infection it should be when the vaccinal immunity is at its height.

NEFF, Kansas City, Mo.

AMYLOID DISEASE IN BONE TUBERCULOSIS, UNCOMPLICATED BY SECONDARY INFECTION: CLUBBING OF FINGERS AND TOES. H. J. SEDDON, Proc. Roy. Soc. Med. **29**:498 (March) 1936.

A boy of 15 years began to complain of lumbar backache, loss of weight, night sweats and breathlessness in March 1932. In April of the same year he had an attack of influenza with bronchitis. After this he was sent to an orthopedic hospital, obviously an ill child. X-ray pictures showed an early metaphysial lesion of the eleventh and twelfth thoracic vertebrae, also a questionable long fusiform abscess extending from the lesion up to the third thoracic vertebra. He was placed on a frame in an open-air ward. A year later irregular pyrexia commenced. There were pain in the right loin and vomiting. The heart and liver were enlarged. There were clubbing of the fingers and slight effusion into both knees. Rigidity of the neck was also present, with a positive Kernig sign, but the cerebrospinal fluid was normal. He improved for a time, but at the beginning of 1934 he became more emaciated, pale and apathethic, and in July of the same year he refused all food; he died on July 6. A summary of the results of postmortem examination accompanies the report. The liver, spleen and kidneys showed extensive amyloid infiltration. There was no evidence of long-standing secondary pyogenic infection.

WILLIAMSON, New Orleans.

HEMATOGENOUS, DISSEMINATED (MILIARY) TUBERCULOSIS WITH RECOVERY. C. HEGLER and H. HOLTHUSEN, Röntgenpraxis **8**:161 (March) 1936.

Of the nine cases reported under the foregoing title, only one is convincing; in this case, although the roentgenographic aspects of the pulmonary infection underwent improvement, the patient died of tuberculous meningitis eighteen months after the apparent onset of the miliary dissemination.

McCUNE, New York.

TUBERCULOUS APPENDICITIS IN A GIRL WITH ACTIVE PULMONARY TUBERCULOSIS: SURGICAL CURE. G. DREYFUS-SÉE, GORECKI and ASCHKANASY, Bull. Soc. de pédiat. de Paris **33**:111 (Jan.) 1935.

A girl 8 years old had diarrhea. Because she had active advanced pulmonary tuberculosis it was thought that she also had intestinal tuberculosis. On physical examination tenderness and rigidity were present in the right lower quadrant of the abdomen. Under local anesthesia the appendix, which was enlarged to the size of the cecum, was removed. It was filled with pus of the consistency of that of a cold abscess. Histologically it showed submucous and subserous hypertrophy with some polymorphonuclear infiltration and an area of caseation with surrounding tubercle formation. It was therefore concluded that the appendix was the seat of an old tuberculous process on which a recent inflammatory reaction had been superimposed. The child recovered from the operation very quickly; her abdominal symptoms disappeared, and her general condition improved.

BENJAMIN, Montreal, Canada.

SYPHILITIC CYSTIC OSTEITIS OF THE FEMUR; FRACTURE AT THIS SITE. E. SORREL and GUICHARD, Bull. Soc. de pédiat. de Paris **33**:117 (Jan.) 1935.

A boy of 13 years sustained a subtrochanteric fracture of the right femur when he fell with very slight violence. Roentgenographic examination revealed a multiloculated cyst at the site of the fracture. The blood test for syphilis was strongly positive, although he showed no signs of the disease, and antisyphilitic treatment was accompanied by progressive healing of the cyst.

BENJAMIN, Montreal, Canada.

EXPERIMENTAL TUBERCULOSIS BY THE PLEURAL ROUTE. A. BOQUET and R. LAPORTE, Compt. rend. Soc. de biol. **118**:741, 1935.

In Guinea-Pigs.—1. In this experiment 0.0001 mg. of bovine tubercle bacilli was injected into the pleural cavity (exposed by operative technic). In from fifteen to twenty days granulations were scattered over the parietal pleura; there was no fluid in the sac; the visceral pleura, the mediastinum and the lungs were free from inflammation; the tracheobronchial and retrosternal glands were enlarged. In from twenty-five to thirty-five days the pleural nodules were increased in number and volume, especially at the site of inoculation; no pleural exudate was noted, but fine granulations appeared on the surfaces of the lung, and the tracheobronchial nodes were caseous. By the end of from fifty to sixty days there was involvement of the mediastinum, pericardial sac (with fluid and effusion into the pleural sac) and subsequently of other organs, as the spleen and liver.

2. With 0.01 and 0.1 mg. of tubercle bacilli, the course to death was much more rapid.

In Rabbits.—1. By injecting identical doses of tubercle bacilli (bovine) into rabbits intrapleurally the same processes were produced as in experiment 1, but these processes were much more rapid in their course.

In Monkeys.—1. By injecting 0.1 mg. of human tubercle bacilli intrapleurally into two monkeys, death was obtained early on the twenty-sixth day, the animals showing granulations of nodular type at the sites of inoculation on the pleurae and over the surface of the right lung; the left lung was normal, and the lymph glands were enlarged. The spleen was swollen. The kidneys and liver were normal. No fluid was found in the sacs. Similar experiments with 0.001 and 0.01 mg. of the bovine strain produced a like picture.

The reaction to tubercle bacilli intrapleurally introduced was different in the three kinds of animals, the lesions progressing more rapidly in the rabbit, and remaining unilateral and much less generalized in the monkey.

WAHL, Cleveland.

THE VIRULENCE OF TWO STRAINS OF TUBERCLE BACILLI ISOLATED FROM SPINAL FLUID AND BLOOD BY THE METHOD OF DE NÈGRE, VALTIS AND VAN DEINSE, IN A CASE OF MILIARY TUBERCULOSIS WITH MENINGITIS. P. ARMAND-DELILLE and H. GAVOIS, Compt. rend. Soc. de biol. **118**:1317, 1935.

The spinal fluid from a 10 year old girl who had miliary tuberculosis with meningitis was injected into guinea-pigs and rabbits according to Löwenstein's method. The guinea-pigs succumbed in six weeks, while the rabbits survived.

Likewise, defibrinated blood was injected by the method of de Nègre (the injection 2 cc. of blood is followed a week later by injections of acetone extract). The rabbits in this series died, while the guinea-pigs survived. All the animals were infected, as shown by the tuberculin test.

The authors wonder at this difference in the virulence of tubercle bacilli in spinal fluid and in blood from the same patient.

WAHL, Cleveland.

A Study of Preventive and Curative Vaccination with BCG. I. Bălteanu, A. Toma and A. Garaguli, Compt. rend. Soc. de biol. **118**:1461, 1935.

A single injection of 5 cg. of BCG vaccine into guinea-pigs conferred resistance to 1 mg. of tubercle bacilli. Repeated ingestion of light doses at twenty-five day intervals did not increase the resistance over that produced by one injection.

Wahl, Cleveland.

Local Immunization of Guinea-Pigs by Intraglandular Injections of BCG. I. Bălteanu, A. Toma and A. Garaguli, Compt. rend. Soc. de biol. **118**: 1465, 1935.

In several series of experiments with injections of BCG vaccine into the suprasternal lymph glands of guinea-pigs, the local resistance in the glands was no greater than in those in animals that had been vaccinated. Caseous tuberculosis resulted.

However, even with smaller doses, the intraglandular BCG immunization gave greater general resistance because the animals thus immunized showed distinctly fewer tuberculous processes viscerally in comparison with the controls.

Wahl, Cleveland.

Fate of Tubercle Bacilli on Reinfection. I. Bălteanu, A. Toma and A. Garaguli, Compt. rend. Soc. de biol. **118**:1467, 1935.

When guinea-pigs which had been inoculated with bovine and human tubercle bacilli subcutaneously and intraglandularly were reinoculated many days later, definite tuberculous lesions, new in type, were produced, as revealed at postmortem examination. The same results were obtained conversely when reinjections were made into the animals from the nodules and the glandular swellings. Reinoculation means, therefore, further and increased infection.

Wahl, Cleveland.

Action of Short Wave Radiations on Experimental Tuberculosis in the Guinea-Pig and on the Resistance of Infected Animals Immunized with BCG. J. Beerens and L. Remouchamps, Compt. rend. Soc. de biol. **119**:85, 1935.

Guinea-pigs were irradiated with waves 5 meters in length—controls and animals immunized with BCG—after all had been given cultures of bovine bacilli. No differences were noted in those immunized and those not immunized, as all showed tuberculous lesions—general in the nonimmunized and glandular in the BCG group.

Wahl, Cleveland.

Researches on Koch's Bacillus in the Milk and Colostrum of Tuberculous Women. I. Petresco, Compt. rend. Soc. de biol. **119**:165, 1935.

Colostrum and breast milk from thirty-nine women who had active pulmonary tuberculosis following delivery of their infants were examined by the culture method and by inoculation of guinea-pigs. No tubercle bacilli were found, which is evidence again that the infection in babies is from the sputum of the infected contacts—that of the mother predominantly.

Wahl, Cleveland.

Tuberculous Allergy and Resistance to Virulent Reinfection in Guinea-Pigs Inoculated by Mouth with Varieties of R and S Forms of BCG. K. E. Birkhaug, Compt. rend. Soc. de biol. **119**:472, 1935.

Series of guinea-pigs protected by oral doses of S and R types of BCG, respectively, showed differences as follows: The tuberculin test was more rapidly

positive in the S group; also, greater immunity was produced by inoculation with the virulent bacilli, the animals living, on the average, eight months, compared with three and a half months for the R group; pathologically, the S group showed less extensive tuberculous lesions.

WAHL, Cleveland.

THE AGE OF FIRST INFECTION WITH TUBERCLE BACILLI IN THE PARISIAN CHILD. P. LEREBOULLET, H. GAVOIS and P. PASQUIER, Rev. de la tuberc. **2**:6 (Jan.) 1936.

A group of healthy Parisian children of from 4 to 14 years were tested by the Pirquet technic to determine the incidence of tuberculous infection at the various ages. The percentages of positive reactions at the various ages were as follows:

Years	Percentage	Years	Percentage
4	8.7	9	47.7
5	25.4	10	44.0
6	33.3	11	46.9
7	34.2	12	55.6
8	35.7	13	75.0
		14	73.1

From these figures it may be seen that the incidence of tuberculous infection is slight up to the fourth year; that it increases rapidly during the fifth and sixth years, then slowly until puberty, when another rapid increase occurs. A comparison of these figures with those of studies made ten years ago reveals that at the present time there is a greatly lessened incidence of infection, especially in the earliest years and up to the age of puberty; in the period of puberty the percentage of infections is practically the same now as it was ten years ago.

The following reasons are offered in explanation of the greatly lessened infection in early childhood. 1. The number of contaminated homes is less, due to lessened morbidity from tuberculosis and also to more general removal of infected persons to sanatoriums. 2. More instruction is given infected persons through various agencies, pertaining to methods of personal hygiene, infants are removed from infected homes and sent to the country, and there is wider application of pneumothorax to ambulatory patients.

As to the influence of preventive vaccination with BCG on these statistics, the authors feel that it remains in the domain of hypothesis and prefer not to discuss it.

The marked increase in infection between 4 and 6 years is obviously due to contact with extrafamilial sources. The child at this age comes in contact for the first time with the outer world in parks, playgrounds and *l'école maternelle*. The susceptible child falls easy prey to the contagion in his new surroundings. From 6 to 11 years, the period of school life, he lives in a more favorable milieu. The provisions made for vacations amid good hygienic surroundings diminish the danger of contagion at this age.

The period of puberty witnesses another acceleration of infection. At this time of rapid growth, physical resistance is diminished. Also fatigue from school work and the added physical burdens of those who must go to work facilitate tuberculous infection and its evolution. No doubt, also the forces favoring decline in the incidence of infection in the earlier years favor delay in the development of the first type of infection with tubercle bacilli.

EUGENE SMITH, Ogden, Utah.

ANTITUBERCULOUS VACCINATION IN THE NEW-BORN. P. CANTONNET and H. CANTONNET, Bol. Inst. internac. am. de protec. a la infancia **9**:297 (Jan.) 1936.

BCG vaccination against tuberculosis can be practiced in the new-born by the subcutaneous and peroral methods of administration. The advantage of the first is that it insures an earlier and more lasting allergic state, with higher standards. The drawback which may be urged against this method is that it causes nodules and abscesses. These are caused, however, only in a small percentage of the subjects.

Every infant vaccinated with BCG at birth should be supervised in children's services, with repeated examinations and consecutive cutaneous tests, with a view to revaccinating if the Pirquet reaction proves negative. If an infant cannot be treated as advised, it should not be vaccinated.

Children who have been vaccinated at birth and who are classifiable into the following groups may yet be infected with the Koch bacillus:

1. Apparently successfully vaccinated infants and infants who have vomited their vaccine, if they live in the immediate vicinity of a tuberculous focus. In such infants tuberculous evolutions common at this age develop.

2. Vaccinated infants who leave the maternity hospital for home in surroundings where there are tuberculous foci, such foci often being met in poor surroundings, owing to the promiscuity in tenements, the frequent changes of domicile and other factors. This group of babies, put in contact with foci of tubercle bacilli before they have arrived at immunity, may show tuberculous evolutions.

3. Children who were vaccinated with BCG at birth and who have lost immunity because they have eliminated the BCG vaccine from their organisms. If they come in contact with bacillus infected subjects, they are sure to become infected. That is why the Cantonnets advise revaccination when the cutaneous reaction proves negative, no matter what time has elapsed since birth.

4. Vaccinated children living in contact with any source of very virulent contagion. Such children may lose immunity during the evolution of any disease which creates an allergic state (e. g., whooping cough). On the other hand, the authors believe that a child infected with the Koch bacillus and presenting a positive skin reaction as the only demonstration of the infection should be isolated as soon as possible from the source of contagion in order to prevent reinfections, and that the same must be done for the vaccinated child, in whom, in spite of evident resistance to bacillary infection, a tuberculous evolution might develop if infection with a large number of organisms occurs over a long period.

LESLIE, Evanston, Ill.

EXPERIMENTAL STUDIES OF THE INFLUENCE OF PREGNANCY ON THE COURSE OF TUBERCULOSIS. W. SCHMIDT-LANGE, Arch. f. Hyg. **115**:221 (Jan.-Feb.) 1936.

Schmidt-Lange points out that despite numerous clinical observations the reciprocal relationships between pregnancy and tuberculosis have not been satisfactorily determined. Both favorable and unfavorable effects have been observed. He points out the difficulties of studying this question by means of experiments on animals. He studied guinea-pigs inoculated with a strain of tubercle bacilli which usually caused a disease lasting twenty months or more. The differences noted between the experimental and the control animals were so slight that it could not be clearly stated that the accompanying tuberculous infection was unfavorably influenced by the pregnancy. So-called apathogenic tubercle bacilli, such as BCG, did not cause tuberculosis in pregnant guinea-pigs and mice. The author believes that his studies check with numerous clinical observations that tuberculosis running a relatively benign course may not be unfavorably influenced by pregnancy. Particular reference is made to the editorial on this subject by Krause (*Am. Rev. Tuberc.* **31**:254, 1935).

GLASER, Rochester, N. Y.

SIGNIFICANCE OF TUBERCLE BACILLI IN STOMACH WASHINGS. E. KRÜGER, Arch. f. Kinderh. **106**:16 (Aug. 13) 1935.

Inoculation of animals with stomach washings from thirty-four children suffering from various forms of tuberculosis gave positive results for seven children. Of these, six had clinically open tuberculosis. Because open tuberculosis could not be demonstrated in the seventh it is argued that tubercle bacilli in the stomach washings do not necessarily come from swallowed sputum but may come through excretion of the bacilli into the stomach during their dissemination by the blood or lymph, or through swallowing bacilli from a primary infection in the lymphoid tissue in the throat.

CRANE, Chicago.

TUBERCULOUS INFILTRATION OF THE LUNG IN CHILDHOOD. K. DIETL and V. KOSZLER, Arch. f. Kinderh. **107**:2, 1936.

The most important criterion of a primary infiltration is proof that the infiltration developed at a time closely corresponding to that of the first infection. The simultaneous occurrence of erythema nodosum speaks with great probability, but not with certainty, for a primary infiltration, since in erythema nodosum not associated with a primary infection perihilar infiltration may occur. Bipolarity of the roentgen shadow speaks for a primary infiltration (with the exception of the very rare bipolarity in nontuberculous pulmonary diseases); absence of bipolarity is not, however, evidence that a primary infiltration is not present. Furthermore, long duration of the shadow is characteristic of primary infection, although primary infiltration of short duration occurs. The development of visibility of the primary complex, associated with recession of the infiltration, permits a conclusion as to a primary complex only if the gradually developing calcification of the primary nodule and of the glands can be demonstrated, since secondary infiltrations may develop in the region of the primary complex. With absorption of a secondary infiltration, the possibility of a nonspecific infiltration must be considered even in children whose reactions to tuberculin are positive. The term "primary infiltration" should be used only for those infiltrations which fulfil the aforementioned criteria. As a rule, however, there is no reason to fail to make the diagnosis. CRANE, Chicago. [AUTHORS' SUMMARY.]

TUBERCULOTOXIC EXANTHEM IN TUBERCULOUS MENINGITIS. D. VON MÓRITZ, Arch. f. Kinderh. **107**:77, 1936.

A case is reported. CRANE, Chicago.

DEPENDENCE OF CUTANEOUS SENSITIVITY TO TUBERCULIN AND TO THE COURSE OF TUBERCULOSIS ON THE THYROID GLAND. A. VIETHEN, Arch. f. Kinderh. **107**:136, 1936.

The dependence of cutaneous sensitivity to tuberculin and of the course of tuberculosis on the presence of the thyroid gland was tested in sixty guinea-pigs. In the determination of the minimal dose of old tuberculin it was shown that sensitivity to tuberculin was higher in animals with than in those without thyroid glands. The sensitivity to tuberculin could not be changed by parenteral administration of thyroxin either in animals with or in those without these glands. The course of tuberculosis was more severe in guinea-pigs without than in those with thyroid glands. CRANE, Chicago. [FROM THE AUTHOR'S SUMMARY.]

CALCIFICATION OF A COLD ABSCESS IN A CASE OF TUBERCULOUS SPONDYLITIS. BARTOLEIT, Röntgenpraxis **8**:169 (March) 1936.

It is uncommon for calcium to appear in the cold abscesses which result from tuberculous infection of the spine. However, when calcification occurs it is to be regarded as a sign of a good prognosis. Bartoleit reports the case of an 8 year old girl suffering from Pott's disease of the lower thoracic portion of the spine. Roentgenographic examination revealed the presence of two calcium-containing cold abscesses, which were located symmetrically on opposite sides of the vertebral column in the region of the kidneys. McCUNE, New York.

TUBERCULOUS MENINGITIS WITH RECOVERY. Y. V. SOLOVEY and I. S. ROZENSVEYG, Vrach. delo **18**:381, 1935.

The authors report two cases of tuberculous meningitis with recovery under high voltage roentgen therapy to the spine.

One patient was 33 years of age. The symptoms were typical of meningitis, and the specific organism was found in the cerebrospinal fluid on two different

occasions. The treatment was started fifteen days after the onset of the illness, and the patient received five courses of high voltage roentgen therapy to the head and spine. He was discharged in good condition three weeks after the beginning of treatment.

The second case was in a child 2½ years of age. The clinical symptoms, though mild, were characteristic of the disease, but the specific organism was found in the cerebrospinal fluid only on one occasion and in very small numbers. The treatment was started twenty days after the onset of the disease. The child slowly improved and five months later was found entirely normal.

The authors believe that the recovery in these cases was not a temporary remission, as in many of the supposedly recovered patients with tuberculous meningitis, as could be judged by the fact that no recurrences were observed in the two patients in the course of one and a half years of observation.

BODER, Los Angeles.

PRODUCTION OF DIPHTHERIA TOXIN WITH A PURE PIG STOMACH DIGEST. C. C. YOUNG, Chinese M. J., supp. 1, February 1936, p. 143.

Young, working at the National Epidemic Prevention Bureau, Peiping, has been following the example of Martin of the Pasteur Institute, Paris, in using an autolysate from pig stomach as an inexpensive but efficient substitute for peptone in producing diphtheria toxin. He gives the methods of preparation, with proposed improvements. The process of preparation is much simpler than that first used by Martin, and the autolysate can be produced at much less cost than with the "infusion-free" peptone medium.

NEFF, Kansas City, Mo.

STUDIES OF B.C.G. CULTURES. F. F. TANG, Chinese M. J., supp. 1, February 1936, p. 186.

At the Henry Lester Institute of Medical Research, Shanghai, two strains of BCG were studied for their effect and efficacy in various animals, including guinea-pigs, rabbits, monkeys, goats, a donkey and a water buffalo. The cultures were well borne by most of the animals. One goat died from local tuberculous lesions, and some of the rabbits and guinea-pigs suffered from the disease. Two monkeys seemed to have been immunized by the subcutaneous vaccination but not by the administration of the material by mouth or through the conjunctiva. The detailed reports of the experiments on animals and of the efficacy of the inoculation are given in this article. Although the question of the use of BCG vaccine in China was discussed, the authors do not mention the advisability thereof.

NEFF, Kansas City, Mo.

DEMONSTRATION OF TUBERCLE BACILLI IN CHILDREN AT A HOSPITAL FOR INFECTIOUS DISEASES BY STOMACH LAVAGE. A. BARFRED, Tr. Scandinav. Tuberc. Cong., 1935, p. 152.

Of 1,013 infants and children who had had acute infectious diseases (279 with positive reactions to tuberculin) and who were examined by means of gastric lavage (with tests on guinea-pigs), 17 were found to harbor tubercle bacilli. To judge from the incidence of tubercle bacilli in the children of school age, one has to reckon with 3 apparently healthy carriers in every class of 30 pupils.

WALLGREN, Gothenburg, Sweden.

PULMONARY TUBERCULOSIS OF BOVINE ORIGIN IN MAN. K. HAMMER, Tr. Scandinav. Tuberc. Cong., 1935, p. 188.

Of 212 strains of tubercle bacilli isolated from persons with open pulmonary tuberculosis at the Aabenraa Sanatorium in Denmark, 20 (9.4 per cent) were of the bovine type (in one instance there was mixed human and bovine infection).

One of the 20 patients from whom bovine bacilli were isolated had a brother at the sanatorium suffering from the same disease but of human origin. Generally the bovine disease was of a malignant type.

WALLGREN, Gothenburg, Sweden.

THE COMPARATIVE DANGER OF DIFFERENT SOURCES OF TUBERCULOUS INFECTION. M. R. HEYNSIUS VAN DEN BERG, Maandschr. v. kindergeneesk. **5**:133 (Jan.) 1936.

Examination of children newly registered at the dispensary of Amsterdam during 1931-1933 (aged up to 14 years) indicated that 3,313 were infected. In a group of infected children consisting of equally large numbers at various ages ("standard group") the percentage with an open source of infection was demonstrated to be 50.8; in a group with positive skin reactions, the percentage was 55.9, and in a group including those who formerly suffered from tuberculosis and those who died, it was 39.2. In the last group the percentage with unaccountable sources of infection was most notable, 47.7, against 24.6 among those who showed only positive skin reactions. The domestic sources of infection (patients with open lesions) were always more frequent than the extradomiciliary ones. When the figures are rearranged and the infections due to contact with patients who had open tuberculosis, in and outside of the home, are compared, the results prove to be equally striking. The investigation showed, however, that, of children in the presence of a domestic source, 35.7 per cent remained infection-free, against 62.3 per cent of those in contact with an extradomiciliary source. The method used at the dispensary is probably responsible for the fact that infections through unknown sources seem to be so serious. At the dispensary the seriously infected children who had contacts with unknown sources come mainly to notice, whereas the more slightly infected ones escape examination. The investigation did not suggest that patients suffering from closed tuberculosis and those who formerly showed positive evidence of the disease but in whom the signs became negative must be classified as untraced sources of infection. Tuberculous lesions in children whose gastric contents contain bacilli must be considered open. As the number of invading bacilli plays an all-important rôle in infection, the potential danger of those lesions in childhood is, in the author's opinion, to be presumed light. Also the comparative frequency of positive skin reactions and negative Schick reactions at different ages does not suggest that children become infected with tubercle bacilli through their playmates. Moreover, the percentage of positive skin reactions appeared to be equally low (16) among the brothers and sisters of a child harboring bacilli in his gastric contents and among the children from homes lodging a person with closed tuberculosis.

VAN CREVELD, Amsterdam, Netherlands.

TUBERCULOSIS OF BONES AND JOINTS. M. H. J. C. THOMASSEN, Maandschr. v. kindergeneesk. **5**:223 (March) 1936.

Thomassen offers a general survey of the nature and of the course of tuberculosis of the bones and joints. There are a number of illustrations.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Blood, Heart and Blood Vessels and Spleen

DISTRIBUTION OF THE ERYTHROCYTE POPULATION IN REGARD TO DIAMETERS AND OSMOTIC RESISTANCE IN SPLENECTOMIZED CASES OF HEMOLYTIC ICTERUS: A CONTRIBUTION TO AN UNDERSTANDING OF THE PATHOGENESIS OF THE DISEASE. G. MOMIGLIANO-LEVI and A. BAIRATI, Am. J. M. Sc. **190**:610 (Nov.) 1935.

The interest here is in the demonstration of an approximate hematologic cure, as represented in the appearance of a persistent normocytic reaction of the mar-

row even in those persons with hemolytic icterus who do not seem to have been completely cured after splenectomy, as evidenced by the persistence of microcytosis and erythrocytic fragility, even though slight. The authors emphasize that "the very rapid stabilization of the biapicality of the curves of red cell diameters and osmotic resistance after splenectomy documents in the clearest manner the capacity of the bone marrow to produce normal cells, at least from the point of view of their diameters. This observation is not favorable to the hypothesis that the spheroidal microcytosis represents a constitutional defect of erythropoiesis." In their opinion, "it is evidence in favor of the view that, with the cessation of hyperhemolysis, that state of affairs disappears which transforms into an actuality the potential disposition of the bone marrow to form pathologic erythrocytes."

HENSKE, Omaha.

THE EFFECT OF CARBON ARC RADIATION ON BLOOD PRESSURE AND CARDIAC OUTPUT. J. R. JOHNSON and others, Am. J. Physiol. **114**:594 (Feb.) 1936.

Following an erythema dose from a carbon arc lamp dogs showed a diminution in both blood pressure and cardiac output. In normal men the blood pressure showed a slight lowering, lasting from one to two days, accompanied by an increase in cardiac output. In persons with hypertension there was consistent and more marked lowering of the blood pressure, accompanied in the majority of cases by increased cardiac output.

NOURSE, Cleveland.

THE ETIOLOGICAL RELATIONSHIP OF AMIDOPYRINE TO AGRANULOCYTOSIS. F. STENN, Illinois M. J. **70**:193 (Aug.) 1936.

Stenn discusses the various reports of agranulocytosis in which it is attributed to use of aminopyrine. He also discusses the various reasons for considering aminopyrine as an important etiologic factor in the disease. In view of the fact that agranulocytosis due to use of this drug is comparatively rare he believes that its occurrence is due to an individual idiosyncrasy for the drug. Since such incidence is relatively rare, and in view of the fact that in a large proportion of cases agranulocytosis is caused by other drugs or conditions, Stenn believes that the profession's present unfavorable attitude toward the use of so valuable an antipyretic and analgesic and so excellent a therapeutic agent in measles lacks an adequate basis and that the ban which some hospitals have placed on its use is unjustified. He thinks that aminopyrine is no more to be condemned than are arsphenamine, bismuth, gold, mercury and silver, all of which act adversely and can be causative of agranulocytosis as well as many other diseases. Like these other drugs, aminopyrine is to be regarded as a very useful medicament but one to which a rare patient may be sensitive.

BARBOUR, Peoria, Ill.

BLOOD TRANSFUSION. R. M. DACUS JR., J. South Carolina M. A. **32**:40 (Feb.) 1936.

The history of transfusion is given, with the indications for its use in a wide range of conditions and the methods.

WESTON JR., Columbia, S. C.

PURULENT PERICARDITIS. L. E. MADDEN, J. South Carolina M. A. **32**:55 (March) 1936.

The literature on this subject is reviewed, and four cases are presented. The patients were under Madden's observation from September 1929 until January 1933. The diagnosis of purulent pericarditis is frequently not made, because it is not thought of or looked for. The treatment is surgical and offers good results.

WESTON JR., Columbia, S. C.

CONGENITAL HEART DISEASE. RENA CRAWFORD, New Orleans M. & S. J. **89**:223 (Nov.) 1936.

The difficulties in diagnosing congenital heart disease are recounted, and the most common conditions producing similar clinical pictures are enumerated. The fact that a fair estimation of the prognosis may be given without a definite anatomic diagnosis being made is justly stressed.

BERKLEY, Los Angeles.

RHEUMATIC PURPURA WITH ABRUPT ONSET BY INTESTINAL HEMORRHAGE. E. CASSOUTE, ZUCCOLI and MONTUS, Bull. Soc. de pédiat. de Paris **33**:144 (Jan.) 1935.

Two boys, one 13 years old and the other 10, suffering from rheumatic purpura, had intestinal hemorrhage at the onset of the disease. Some time later, twenty days in one case, abdominal pain and petechial and urticarial lesions of the skin developed. Both had persistent tachycardia. Both slowly but completely recovered.

BENJAMIN, Montreal, Canada.

SEVERE ANEMIA IN AN INFANT FED EXCLUSIVELY WITH GOAT'S MILK FOR SIX MONTHS. LOUISE WEILL, Bull. Soc. de pédiat. de Paris **33**:145 (Jan.) 1935.

A puny infant 9 months old had been breast fed for three months and then given only goat's milk for six months. She had marked hypochromic anemia. It is pointed out that iron did not help the condition until the goat's milk was withdrawn from the diet and cow's milk substituted for it. No explanation is offered for this peculiar anemia, which was reproduced in guinea-pigs, but it is not thought that it was due to undernourishment or to deficiency in vitamin C or in iron. The infant was given iron as well as liver extract and viosterol after cow's milk was substituted for goat's milk, and she made a good recovery.

BENJAMIN, Montreal, Canada.

PRIMARY RHEUMATIC ENDOCARDITIS IN A CHILD. J. CATHALA, J. SUSTENDAL and G. PATEY, Bull. Soc. de pédiat. de Paris **34**:187 (March) 1936.

A boy 22 months old had vague pain in the legs at the onset of an illness during which he had a fever intermittently for about a month. He showed some anemia, and an apical systolic murmur developed. As soon as he was given sodium salicylate, the temperature became normal. When examined two years later he had cardiac enlargement and a loud blowing systolic murmur. In the interval he had frequently complained of pain in the limbs, which was always relieved by taking salicylates. The onset of rheumatic disease at such an early age and the insignificant pain in the limbs for only a very short time are the reasons for reporting the case.

BENJAMIN, Montreal, Canada.

RELATIONS OF THE BLOOD CORPUSCLE VOLUME IN THE ANEMIA DUE TO FEEDINGS OF GOAT'S MILK TO GROWING RATS. H. KELTING, Arch. f. Kinderh. **104**: 212 (March 29) 1935.

The anemia produced in growing rats by feeding them goat's milk shows the same relation between the volume of the blood corpuscles and the color index as observed in anemias of the pernicious type. The onset of anemia of the pernicious type in rats cannot, however, be recognized by determining the volume and index as in human patients, since the characteristic changes from normal values become striking only with severe anemia.

CRANE, Chicago.

DELAYED EVACUATION OF THE STOMACH ACCOMPANYING ARTERIAL HYPOTONIA IN CHILDHOOD. E. HAINISS and G. SURÁNYI, Arch. f. Kinderh. **105**:219 (July 16) 1935.

Of forty children with low blood pressure, thirty-five were found to have delayed evacuation of the stomach. Reversely, a high proportion of children recognized as having a disturbance of the evacuation of the stomach showed continuous low blood pressure. Both findings are interpreted as symptoms of disturbance in the function of the vegetative nervous system. CRANE, Chicago.

STUDIES OF THROMBOCYTE COUNTS IN CHILDHOOD. FRITZ BECKER, Arch. f. Kinderh. **107**:230, 1936.

Thrombocyte counts were made on the blood plasma of 300 normal children from 3 weeks to 16 years of age by Jürgens' direct method, based on skin puncture, and an average of 575,000 per cubic millimeter was found. The counts on children in the first and second year were about 100,000 higher. At this age the percentage of children who exceed the usual limits of normal is much greater than it is in later childhood, without the observation of any change in bleeding or in coagulation time.

A satisfactory simplification of the procedure consists in using for the thrombocyte count the plasma obtained during a determination of the sedimentation time according to Linzenmeier's method. Jürgens' direct method of counting the thrombocytes is materially more exact than Fonio's indirect method (on smears), and it is therefore the method of choice. CRANE, Chicago.

RESULTS OF BLOOD TRANSFUSIONS IN 1,242 CASES. A. FILATOV and others, Beitr. z. klin. Chir. **161**:309, 1935.

Best results were obtained in cases in which loss of blood was severe. Transfusion of blood was also found to aid in preoperative and postoperative treatment and also in the treatment of blood disease. It was also helpful at times in the treatment of poisoning. But in severe infections blood transfusions were not satisfactory; there was a mortality rate of 63 per cent in spite of blood transfusion. The various methods used and the number of cases are as follows: direct transfusion in 402, transfusion of citrated blood in 554, transfusion of preserved blood in 242 and reinfusion of blood in the treatment of patients with abdominal disease in 44.

The last method gave excellent results in cases of acute severe loss of blood. RUBIN, Boston.

THE IODOPHILIC SUBSTANCE IN LEUKOCYTES. A. GIRARDIN, Jahrb. f. Kinderh. **145**:140 (Sept.) 1935.

Following a discussion of the staining technics for the demonstration of an iodophilic substance in leukocytes, Girardin gives the results of his studies. His results for the most part confirm the findings of previous investigators: Normally about 20 per cent of the neutrophils contain iodophilic granules. In septic conditions the percentage is increased; in one case of empyema about 90 per cent of the neutrophils contained granules of this type. The iodophilic reaction is present with leukocytosis but is not necessarily parallel. It is present at times with leukopenia. With secondary (posthemorrhagic) anemias there is a decrease, and with primary anemias there is an increase. In dyspepsia and dystrophies the height of the iodophilic curve is much less than normal, as also in pyloric stenosis. A case of diabetes mellitus was studied. There was a slight increase in the iodophilic substance, which remained uninfluenced following the use of insulin.

One hour after a meal the increase in the granular leukocytes is maximal. Within about three hours or later the percentage sinks to the fasting level.

Studies of the blood sugar were made. The height of the blood sugar curve was found to correspond with the height of the increase in iodophilic leukocytes.

The author was unable to confirm the observation made by previous investigators that cells other than polymorphonuclear neutrophils were carriers of these granules.

LANDAU, Hannibal, Mo.

HEART BLOCK (MORGAGNI-ADAMS-STOKES) IN A CHILD ONE AND A HALF YEARS OLD. A. FLESCH, Orvosi hetil. **80**:806 (Aug. 22) 1936.

An 18 month old child was brought to a children's hospital in Budapest with the complaint of fever of one day's duration. The physician had found angina, but the child had fainting attacks. The temperature was not high (38 C. [100.4 F.]). Over the heart there was a systolic murmur. The pulse rate was 48. On the following day the child had several fainting attacks, the skin was cyanotic, heart sounds were not heard, and the pulse was not palpable. The attacks lasted from one to two minutes. Electrocardiographic examination showed that every third auricular contraction was followed by one ventricular contraction. The T wave disappeared, and extrasystoles were present. Between the auricular and the ventricular contraction no connection was to be found; a complete atrioventricular block developed.

The state improved later, the child receiving racemic ephedrine steadily. The body development later was normal, and the child now seems to be healthy. The electrocardiogram shows that the T waves have reappeared, that the extrasystoles have disappeared, but that the heart block is complete and definite.

Flesch believes that severe myocarditis developed after angina and that in connection with it the bundle of His was injured.

GÖTTCHE, Budapest, Hungary.

PERIDENTAL CHANGES IN SPLENOMEGALY OF THE GAUCHER TYPE. CHARLES BREUER, Zubni lék. **35**:58 (Feb.) 1935.

Four cases of Gaucher's splenomegaly are cited in which changes in the peridental area were noted. These changes were inflammatory or dystrophic in character. It is felt that the changes were part of the general systemic reaction and did not represent a specific peridental reaction.

STULIK, Chicago.

A PROBABLE CASE OF PAROXYSMAL TACHYCARDIA IN A BABY. J. M. SOETERS, Maandschr. v. kindergeneesk. **5**:167 (Jan.) 1936.

An infant of 4 months had a pulse rate of about 300 beats per minute. The etiologic factors are unknown. The therapy consisted in repeated intramuscular injections of quinine sulfate and intravenous injections of ouabain. Complete recovery followed.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Nose, Throat and Ear

MASTOIDITIS IN THE INFANT. M. GUILLEMOT and others, Bull. Soc. de pédiat. de Paris **34**:136 (March) 1936.

A discussion of the problems of diagnosis of mastoiditis in infants is reported. Some of the discussers are more radical than others, but on the whole all are agreed that the condition may be present without obvious signs of otitis media. Despite this fact and the fact that antrotomy in an infant is a relatively simple procedure, one should be very careful not to subject an infant to an operation in which a normal mastoid antrum is opened. Better and more intensive roentgenographic examination is mentioned as offering a possible development for more accurate diagnosis in the future.

BENJAMIN, Montreal, Canada.

After-Treatment of Tracheotomized Children. E. von György, Arch. f. Kinderh. **104**:208 (March 29) 1935.

After tracheotomy in a child the following points are important: (1) immunization against diphtheria, (2) prophylactic treatment against pneumonia, (3) keeping the cannula clean at all times, (4) prevention of drying of secretions in the cannula and (5) earliest possible removal of the cannula.

Crane, Chicago. [From the Author's Summary.]

Disease of the Accessory Cavities in Infancy. Hildegard Schönberg, Arch. f. Kinderh. **107**:216, 1936.

Of 232 infants examined post mortem, 154 showed empyema of the middle ear, of the antrum of Highmore or of both. Of 76 infants who had had dyspepsia, 57 disclosed infections of these cavities. Another common observation in the infants who had had dyspepsia was that, in addition to parenchymatous clouding of the liver, they had a more or less marked peripheral fatty degeneration of the liver. This raises the question whether the injury of the liver was a cause or a result of the nutritional disturbance. The most probable sequence is as follows: As the result of a cold there develops an infection of the accessory nasal cavities, which runs a slow course but eventually leads to injury of the hepatic parenchyma, which then produces nutritional disturbance.

Crane, Chicago.

Tracheal Sarcoma in a Child. L. Abbate, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **140**:179, 1935.

Abbate reports the clinical history of a girl aged 10 who suffered from increasing dyspnea. Tracheoscopy revealed a spherical tumor above the bifurcation. After the proper tracheal tubes had been constructed, tracheotomy was done. After it had been determined that the tumor was 8.5 below the lower rim of the tracheotomy wound, the tumor was removed piece by piece by means of curets while the patient was in Trendelenburg's position. The histologic examination of the removed tissues revealed sarcoma. It was decided to resort to after-treatment by means of radium. A special container was constructed which permitted free passage of air around the capsule containing the radium. The radium was introduced for from forty-five to sixty minutes at a time. Twelve treatments were given. After six treatments the rather bumpy surface from which the tumor had been removed could no longer be differentiated from the surrounding swollen and reddish tissue. Nine months later the examination revealed a circular zone of shiny brownish red tissue which appeared atrophic; that is, it resembled the mucous membrane in pharyngitis sicca. Tracheoscopy from time to time disclosed no recurrences.

Editor's Abstract. [Arch. Otolaryng.]

Clinical and Pathologic Aspects of Tonsillotomy. J. Jeschek, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **140**:197, 1936.

Jeschek points out that although in the last three decades tonsillectomy has become more customary, tonsillotomy was still often resorted to in cases in which the tonsils were only hypertrophic. To be sure, it was early pointed out that tonsillotomy favors the development of tonsillitis and of inflammation of the cervical glands and that a large percentage of patients who underwent tonsillotomy were subject to rheumatic, polyarthritis and myocarditic processes. The author reports observations on twenty patients who underwent tonsillotomy about eight years before examination. He found that all of them had a predisposition toward tonsillitis and that thirteen had severe local or general complications. The tonsils of sixteen were subjected to histologic examination, and it was found that in nearly all of them there existed chronic atrophic tonsillitis, with severe cicatrization, cysts and inflammatory reactions. The examination of tonsils which were

removed shortly after the tonsillotomy revealed that the changes which seem to be the causes of the frequent disorders in tonsillar stumps are the direct result of tonsillotomy. The favorable results of the total removal of the tonsillar remnants indicate that tonsillectomy is the better method.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

OTOMICROSCOPIC STUDY OF TYMPANIC MEMBRANE IN MASTOIDITIS. E. LÜSCHER, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **140**:355, 1936.

Lüscher says that in 1926 Steinmann called attention to a peculiar aspect of the tympanic membrane in mastoiditis when this is ripe for operation. He pointed out that in mastoiditis the tympanic membrane is characterized by pale red hyperemia as compared with the bright red hyperemia in uncomplicated acute otitis media. Lüscher shows that otomicroscopic examination by means of his otomicroscope corroborates and further clarifies Steinmann's observations, for a tenfold to twentyfold magnification reveals, in addition to the characteristic color, several other typical changes. He elucidates these on the basis of three case reports with illustrations. He reaches the conclusion that in mastoiditis the changes in the tympanic membrane which he has mentioned appear only in some of the cases of empyema of the mastoid and that consequently their absence does not definitely exclude mastoiditis that is ripe for operation. However, if the changes described are present they indicate not only mastoiditis but also empyema. For this reason, the changes are especially important in latent mastoiditis, for they indicate the necessity of antrotomy.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

ALTERATION OF THE BACTERIAL FLORA OF THE TONSILS IN THE COURSE OF ROENTGEN THERAPY FOR CHRONIC TONSILLITIS. E. D. DUBOVY and N. M. GORDIAN, Fortschr. a. d. Geb. d. Röntgenstrahlen **53**:73 (Jan.) 1936.

Roentgen therapy produced a decrease in the number of persons whose throats harbored pathogenic organisms. In a group of fourteen children whose tonsils were large but who exhibited no associated symptoms of infection, pathogenic organisms were not recovered either before or after treatment. The experiment was entirely uncontrolled.

McCUNE, New York.

PARANASAL SINUSITIS IN CHILDREN. H. LEICHER, Med. Klin. **32**:273 (Feb. 28) 1936.

Leicher discusses the diagnosis, prognosis and treatment of sinusitis in children, without contributing information which may not be found in standard textbooks. He adds the following table compiled from measurements which he made from roentgenograms and at operation and necropsy, but he does not say on how many persons these values are based.

Age	Dimension Measured	Maxillary Sinus, Mm.	Frontal Sinus, Mm.	Ethmoid Sinus, Mm.		Sphenoid Sinus, Mm.
				Anterior	Posterior	
New-born	Height	3-7	0	2-5	2-5	0-2
	Width	2-4	0	1-3	1-2	0-2
	Depth	7-12	0	2-5	3-5	0-3
1 year	Height	4-8	0	2-6	2-6	1-3
	Width	3-7	0	2-3	2-3	1-2
	Depth	7-18	0	2-7	3-10	1-4
2 years	Height	5-9	0-3	3-8	3-8	2-3
	Width	3-8	0-2	2-3	2-4	2-3
	Depth	9-20	0-2	3-7	3-10	2-5
4 years	Height	8-15	0-4	3-10	3-10	3-5
	Width	6-12	0-3	2-4	2-4	2-3
	Depth	15-24	0-4	3-8	4-11	2-5
8 years	Height	15-24	0-8	6-12	4-10	5-10
	Width	10-18	0-8	3-6	3-5	3-6
	Depth	20-30	0-5	5-8	8-18	7-12

DOOLEY, New York.

TONSILLOGENIC SEPSIS. G. HOFER and F. X. KOCH, Monatschr. f. Ohrenh. **69:** 1409 (Dec.) 1935.

Hofer and Koch analyze a series of 854 cases of tonsillar disorder. In nineteen patients surgical intervention became necessary. Eleven of these patients were cured by simple tonsillectomy of the type performed for abscess. In three patients with cervical phlegmon without hematogenous sepsis cervical mediastinotomy was effective; in one with gas phlegmon the condition terminated fatally as the result of arrosion of the superior thyroid artery and of the lingual artery. Four cases of tonsillogenic sepsis which are interesting from the point of view of onset and therapy are reported in detail. Only one of the four patients, all of whom had severe attacks of chills, could be saved, and in this patient surgical treatment had been instituted after the first attack of chills. The other three patients were not hospitalized until after several attacks of chills had passed and after the general condition had already been greatly impaired. The authors stress that the surgical procedure for tonsillogenic sepsis can be successful only if it is instituted early, that is, at the earliest stage of propagation. With every attack of chills the prognosis becomes considerably more unfavorable, for a hematogenous dissemination involves particularly the pulmonary vessels, and pneumonia with the formation of abscesses and with septic toxic impairment is the result. The authors point out, further, that in many cases reported in the literature in which the condition is designated as sepsis it does not deserve this term. A high temperature alone is not sufficient for a diagnosis of sepsis as long as the other clinical symptoms, such as chills, small, fluttering and frequent pulse, great impairment of the general condition and acute metastases, are absent. If severe sepsis is confused with acute tonsillar infection, accompanied by high temperature, it is impossible to get a clear insight into the value of the various surgical methods.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TONSILLOGENOUS SEPSIS. F. J. MAYER, Monatschr. f. Ohrenh. **69**:1415 (Dec.) 1935.

Mayer says that many years of experience and careful study indicate that surgical treatment is advisable for tonsillogenous sepsis. He mentions four phases of surgical treatment: (1) tonsillectomy, (2) opening and tamponade or drainage of the parapharyngeal and retropharyngeal spaces, (3) exposure of the vascular sheath and ligation of the jugular vein and, if necessary, extirpation of the glands and (4) mediastinotomy. Depending on the differences in the various cases, one or more of these procedures may be dispensed with. The author thinks that tonsillectomy is advisable in all cases. However, in those of cervical phlegmon with abscess formation, it may have to be postponed. Moreover, the order of the four phases may have to be different.

In discussing the ligation of the jugular vein, Mayer points out that except in demonstrated thrombophlebitis the value of this form of intervention is still disputed. He says that under the direction of Professor Marschik a way out is found in the form of the preliminary passing of strips of iodoform gauze under the vessel. The ligation as such is postponed until the disease process indicates it. Moreover, this preliminary passing of the gauze under and around the vessel frequently effects a partial closure of the jugular vein and thus fulfils the purpose of the ligation; yet the blood stream is not permanently interrupted. The author regards the opening of the parapharyngeal and retropharyngeal spaces as the most important phase of the surgical treatment of tonsillogenous sepsis. He thinks that this phase and tonsillectomy should never be omitted. In the concluding summary he emphasizes that surgical treatment should not be the last resort but should be instituted as early as possible. Particularly if ligation of the jugular vein is done with reservation and caution as suggested, surgical treatment does not involve mutilation and thus should be done with less hesitation.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

EFFECTS OF ACID AND ALKALINE DIETS ON TONSILS. H. HOEPKE and W. GRÜNING, Ztschr. f. Hals-, Nasen- u. Ohrenh. **37**:396, 1935.

Hoepke and Grüning made their studies on hedgehogs just after the animals awakened from five months of hibernation. The size and the histologic aspects of the tonsils during hibernation were known from former studies. It was found than an alkaline diet causes considerable shrinkage of the tonsils (by about a third). The number of nodules is greatly reduced, and there are profuse formation and elimination of small lymphocytes. The lymph vessels that empty into the organs show profuse filling. After an acid diet, the tonsils decrease only slightly from their size during hibernation, and the number of nodules is slightly reduced. The formation of small lymphocytes is greatly inhibited and the formation of large cell forms increased. For this reason, the centers of the nodules are rather conspicuous. The discharge of small lymphocytes into the organism ceases or is only slight. In trying to explain this differing behavior, Hoepke and Grüning point out that the acid diet is nearer to the natural diet of the hedgehog than is the alkaline diet. In accordance with this, the reaction of the lymphatic system is less with the acid diet than with the alkaline diet. The latter elicits a spontaneous defense or a counter attack in the lymphatic system.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

HEREDITARY ATROPHY OF THE ACOUSTIC NERVE. N. A. POPOV, Ztschr. f. Hals-, Nasen- u. Ohrenh. **37**:407, 1935.

Popov points out that the disorder under consideration is not so well known under the term applied to it here as under such terms as "congenital deafness" or "congenital deafmutism," "heredodegenerative deafness or baryecoia," "labyrinthine baryecoia of young persons" and "progressive labyrinthine deafness or baryecoia," all of which have been combined under the general term "heredopathia acustica." He reports on two members of a family with hereditary deafness. He gives a diagram of the genealogical tree and discusses the anatomic aspects of congenital deafness. After citing the opinions of other investigators regarding the mode of hereditary transmission, he says that on the basis of present knowledge the hereditary transmission of congenital deafness may be according to the recessive as well as to the dominant type. His own observations seem to indicate this. Moreover, the alcoholism in the family studied by him may be regarded as hereditary narcomania. It is possible that the concurrence of the two disorders is not entirely accidental; the chronic alcoholic intoxication of the ancestors of this family might have caused the hereditary disease of the auditory nerve, particularly since it is known that alcoholism may be related to various neuropathies and psychopathies.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

STERILE ANIMAL PLASMA AS A HEMOSTATIC AGENT AFTER TONSILLECTOMY. A. TOBECK, Ztschr. f. Hals-, Nasen- u. Ohrenh. **37**:463, 1935.

Tobeck resorted to the use of sterile coagulable animal plasma in twelve cases of hemorrhage after tonsillectomy. He injected it into the peritonsillar tissue near the site of bleeding. The hemorrhage was promptly controlled in all but one of the cases. The one failure was ascribable less to the treatment than to the faulty technic. For the control of less severe hemorrhage 1 ampule of animal plasma was usually adequate, but when hemorrhage was severe 2 ampules were administered. The chief advantages of the use of animal plasma are these: 1. The administration is simple. 2. It is practically painless and thus does not tax the weakened patient. 3. The action of the plasma is quick and reliable. 4. The plasma is harmless.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

THE PART OF OTITIS IN INFANCY. E. GYÖRGY, Orvosi hetil. **80**:143 (Feb. 15) 1936.

In infancy otitis media may cause not only local but also general symptoms. It may cause symptoms of dehydration. In this case incision of the drum is not enough; an antrotomy should be done. Antrotomy should be done also in cases of chronic otitis media, because the permanent absorption of pus may poison the body permanently.

GÖTTCHE, Budapest, Hungary.

SIGNIFICANCE OF OTITIS MEDIA AND MASTOIDITIS IN INFANCY. J. CSAPÓ, Orvosi hetil. **80**:284 (March 28) 1936.

In infancy otitis media cannot be regarded as a local illness, because it may cause general symptoms, especially dehydration. The incision of the drum is not enough; mastoidectomy should be performed. The fact that manifest mastoiditis does not always cause toxic symptoms does not speak against the fact that occult mastoiditis cannot cause toxic disorders. The extent of the focus is not in proportion to its effect.

GÖTTCHE, Budapest, Hungary.

Diseases of Lungs, Pleura and Mediastinum

COMPARISON OF PATHOLOGIC CHANGES OF INFANTILE ASTHMA WITH ASTHMA OF LONG DURATION. G. L. WALDBOTT, J. Allergy **7**:264 (March) 1936.

The pulmonary changes associated with asthma of short and of long duration as observed at autopsy are compared. One case was that of a child 6 months old who had had asthma for three weeks; another was that of a child of 3 months with asthma of six weeks' duration. In each case there was a family history of allergy.

The lungs showed little emphysema, little mucus, no hypertrophy of muscle of the bronchi and no hyperplasia of mucous glands. There was capillary congestion in the alveoli along with edema, extravasation of blood, degeneration of alveolar cells and traumatic emphysema alternating with atelectasis. The lymph follicles were markedly hyperplastic.

Death was probably due to edematous hemorrhagic lesions and bronchopneumonia rather than to obstruction of the bronchi with mucus as in the adult.

Waldbott tells that the changes observed at auotpsy resemble those of anaphylaxis more closely than those of asthma of long duration.

HOYER, Cincinnati.

EFFECTS OF HELIUM MIXED WITH OXYGEN ON THE MECHANICS OF RESPIRATION. A. L. BARACH and M. ECKMAN, J. Clin. Investigation **15**:47 (Jan.) 1936.

Experiments to determine the effect of helium mixed with oxygen on certain types of dyspnea were performed on normal human subjects and on dogs anesthetized with pentobarbital sodium. The subjects were made to breathe varying mixtures of gases, under different conditions, through constricted orifices of varying size. In summary, helium decreased the effort of the respiratory musculature and, as to its physical function, lowered intrapleural pressure. Oxygen administered in increasing concentrations decreased the pulmonary ventilation and, as a chemical factor, lessened the work of respiration. The presence of nitrogen was detrimental in that it was useful neither physically nor chemically. A mixture of from 30 to 35 per cent oxygen with from 65 to 70 per cent helium seemed to be of greater benefit than other combinations. The application of these findings to clinical conditions (asthma and obstructive lesions in the trachea and larynx) and their general bearing on the concept of dyspnea are discussed.

GUEST, Cincinnati.

TRAUMATIC MEDIASTINAL EMPHYSEMA WITHOUT FRACTURE OF A RIB IN A CHILD. E. SORREL and GUY, Bull. Soc. de pédiat. de Paris **33**:114 (Jan.) 1935.

A boy 3 years old was injured in an automobile accident. He showed marked dyspnea. The right clavicle and the upper part of the right humerus were fractured, but the ribs and sternum were not. There was subcutaneous emphysema in the suprasternal and left supraclavicular regions. There was no pneumothorax, and it is believed that the condition was mediastinal emphysema following thoracic contusion without fracture of a rib and that it was due to rupture of small bronchioles and alveoli and of the overlying pleura in the region of the mediastinum. The respiratory distress gradually lessened, and the condition cleared up spontaneously.

BENJAMIN, Montreal, Canada.

FOREIGN BODY IN A BRONCHUS SPONTANEOUSLY EXPELLED THROUGH AN INTERCOSTAL SPACE. FERRU and DUCOS, Bull. Soc. de pédiat de Paris **34**:177 (March) 1936.

A boy 8 months old was seized with a choking spell while seated in a garden in the afternoon. When examined that night, he had dyspnea, cyanosis and high fever but no positive physical findings in the chest. Fifteen days later an inflammatory swelling which had been present for a few days over the eighth right intercostal space opened, and the stalk of a barbed weed was expelled along with a few drops of serous fluid. There were a small area of dulness and distant blowing breathing under the swelling in the soft tissues. It is pointed out that spontaneous expulsion of a weed of this type through an intercostal space, though rare, has been reported by a number of observers previously and that it invariably has occurred on the right side.

BENJAMIN, Montreal, Canada.

CHRONIC MULTILOCULAR ABSCESS OF THE LUNG IN A CHILD. FERRU, DUCELLIER and SAVIN, Bull. Soc. de pédiat. de Paris **34**:180 (March) 1936.

A boy 11 years old had a large multilocular abscess in the upper lobe of the left lung. It seemed to have developed insidiously. Bronchoscopic aspiration was performed, and a very large quantity of pus was withdrawn, from which streptococci grew on culture. Two years later a large cavity containing a small amount of fluid was still present despite vaccine and other therapy. His general condition remained good.

BENJAMIN, Montreal, Canada.

ABSCESS OF THE LUNG DUE TO PFEIFFER'S BACILLUS. H. GRENET and J. PATEL, Bull. Soc. de pédiat. de Paris **34**:193 (March) 1936.

A boy 12½ years old had an abscess in the upper lobe of the right lung for about three months. There was no communication with the bronchus. Aspiration was performed and pus obtained, from which the bacillus of Pfeiffer was isolated. Pneumotomy was done in two stages, and the condition was cured. When seen three years later, the boy was well.

BENJAMIN, Montreal, Canada.

PROGNOSIS AND TREATMENT OF EMPYEMA IN INFANCY. ISTRÁN FLESCH, Arch. f. Kinderh. **107**:193, 1936.

In cases of hyperacute empyema in infancy not secondary to pneumonia the prognosis is most unfavorable, for the empyema is often unrecognizable and consequently untreated. Spontaneous recovery may occur in cases in which the exudate is of small amount.

Regardless of the cause, the best therapeutic results are obtained from systematic punctures. Intrathoracic lavage is sometimes necessary for mechanical

reasons. Operative intervention is resorted to only after conservative treatment has been unsuccessful. Simple thoracotomy under local anesthesia and drainage through a rubber tube constitute the preferred operative procedure. General care of the infant and supportive measures are emphasized. CRANE, Chicago.

PULMONARY ABSCESSES IN CHILDREN. R. PRIESEL, Arch. f. Kinderh. **107**:204, 1936.

Postpneumonic abscess of the lung in childhood has a very good prognosis with purely conservative treatment, limited to improvement of the general condition and of resistance. In over twenty cases of postpneumonic abscess of the lung healing nearly always occurred. Abscesses caused by foreign bodies require, of course, special treatment. Abscesses, often multiple, occurring as metastases via the blood stream from a focus of infection have a very serious prognosis, although children with even severe abscesses of this type may survive. CRANE, Chicago.

CONGENITALITY AND HEREDITY OF BRONCHIECTASIS. M. KARTAGENER, Ergebn. d. inn. Med. u. Kinderh. **49**:378, 1935.

On the basis of his observations in 142 cases of bronchiectasis, as well as on that of a study of the literature, Kartagener inclines to the belief that bronchiectasis is a congenital condition, for the following reasons: 1. There is a striking predilection for certain lobes of the lungs (the left lower and the right upper and middle lobes). 2. Pathologico-anatomic investigations of bronchiectasis show absence of elastic fibers in the bronchial wall despite complete absence of inflammatory processes. This absence of elastic tissue is the histologic expression of the so-called idiopathic bronchiectasia ("default original" of Bard). The so-called acquired bronchiectasis, however, is the result of destructive processes (abscesses or grangrene) within the parenchyma of the lung and thus is not to be classed as true bronchiectasis. 3. One frequently finds other anomalies and areas of malformation of the respiratory system in patients suffering from bronchiectasis. The fact of the multiplicity of malformations, well known in the realm of pathology, is further confirmed by the striking frequency of bronchiectasia in cases of situs inversus viscerum. 4. The occurrence of the condition is familial; this fact has been observed in thirteen families, in four of which twins were involved.

Kartagener concludes with the remark that even if one does not doubt that bronchiectasis may be acquired one must admit as a result of a consideration of the aforementioned reasons that congenital bronchiectasis is of much more frequent occurrence than has hitherto been assumed. CAPPER, Philadelphia.

CHANGES IN THE NUMBER OF EOSINOPHILIC CELLS AFTER INJECTION OF EPINEPHRINE INTO CHILDREN WITH BRONCHOPNEUMONIA. T. KROMPASZKY, Orvosi hetil. **80**:56 (Jan. 18) 1936.

The count of eosinophilic cells was made by Dunger's method. Infants received 0.10 cc.; children from 1 to 2 years old, 0.20 cc. The counting was done at one-half hour, one and a half and two and a half hours after injection. Krompaszky could not find any connection between the behavior of the eosinophils and the outcome of the illness. GÖTTCHE, Budapest, Hungary.

PARADOXICAL ROENTGEN SHADOWS IN PNEUMOTHORAX. F. FLEISCHNER, Fortschr. a. d. Geb. d. Röntgenstrahlen **53**:45 (Jan.) 1936.

In many cases of artificial pneumothorax the portion of the lung field which one would expect to be entirely translucent is obscured by a more or less dense shadow, while medial to this zone, lying between it and the dense shadow of the

collapsed lung, is a brightly lighted area. By means of cleverly constructed diagrams Fleischner shows that the paradoxical shadow results from incomplete collapse of the lung, combined with thickening of the parietal pleura. The technic of schematic representation which is employed in this paper deserves favorable comment.

McCUNE, New York.

THE ANATOMIC BASIS OF THE LINEAR SHADOWS (*Begleitstreifen*) OBSERVED ALONG THE LATERAL CURVATURE OF THE MIDDLE AND LOWER RIBS (LAMELLAR PLEURISY). W. NEUGEBAUER and A. KUBAT, Fortschr. a. d. Geb. d. Roentgenstrahlen **53**:53 (Jan.) 1936.

Anatomic studies demonstrate clearly that the thin linear shadows which are seen along the lateral aspect of the inner wall of the chest and which have frequently been ascribed to disease of the pleura are more often due to the presence of normal structures. The most important of these are the fat pads which line the outer surface of the parietal pleura. The thickened peripheral zone of such shadows is the result of the fact that both the parietal and the visceral pleura are recorded tangentially.

McCUNE, New York.

A CASE OF CONGENITAL ABSENCE OF THE LEFT LUNG. M. LÜDIN and A. WERTHEMANN, Fortschr. a. d. Geb. d. Röntgenstrahlen **53**:273 (March) 1936.

An elderly woman was thought during life to be suffering from either massive collapse or extensive cicatricial contracture of the left lung. The opinion was based on: a history of frequent cough and recurrent dyspnea since childhood; dulness and diminution in breath sounds over the left side of the chest together with displacement of the heart to the left, and roentgen evidence of collapse of the left lung. In addition, auscultatory findings suggested congenital malformation of the heart. Autopsy at the age of 58 years revealed absence of the entire left lung; in place of the lung some rudimentary fibrous tissue was present. A congenital anomaly of the great vessels was demonstrated. The literature indicates that there have been only three similar cases in which the diagnosis was confirmed at autopsy; the literature contains the reports of four cases in which the diagnosis rested on clinical evidence alone. The characteristic roentgenographic features are: homogeneous increase in density of the affected side with displacement of the mediastinum toward the same side; immobility of the diaphragm on the affected side; herniation of the intact lung into the affected half of the thorax; asymmetry of the angles made by the ribs on the two sides and the sagittal plane of the body, with narrowing of the interspaces on the side from which the lung is missing. These characters are not pathognomonic; even the use of bronchography will not serve to distinguish this condition from acquired bronchial stenosis. A carefully taken history of great importance. Congenital absence of a lung is to be regarded as a developmental defect concerning which numerous explanatory hypotheses have been advanced. It is not infrequently associated with developmental anomalies of the great vessels.

McCUNE, New York.

A PARTICULAR CASE OF PULMONARY ATELECTASIS IN A BABY. A. DEKKER-JONKER, Maandschr. v. kindergeneesk. **5**:215 (Feb.) 1936.

An infant of 5 weeks presented pronounced atelectasis of the right lung with compensatory emphysema of the left lung. This condition had given rise to dextrocardia. The child had several attacks of cyanosis and dyspnea. Post mortem the atelectasis was found to be caused by an obstruction of the right main bronchus by a mass of pus and mucus, probably aspirated during birth.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Gastro-Intestinal Tract, Liver and Peritoneum

LIVER FUNCTION AS TESTED BY THE LIPEMIC CURVE AFTER INTRAVENOUS FAT ADMINISTRATION. A. NACHLAS, G. L. DUFF, H. C. TIDWELL and L. E. HOLT JR., J. Clin. Investigation **15**:143 (Jan.) 1936.

Carbon tetrachloride administered to dogs caused difficulty in the removal of intravenously injected fat from the blood. It was suggested that the lipemic curve after the intravenous injection of fat might be of value in the study of liver function.

GUEST, Cincinnati.

MORTALITY FACTORS IN ACUTE APPENDICITIS (STUDY OF ONE THOUSAND CASES). E. D. LEONARD and S. DEROW, New England J. Med. **214**:52 (Jan. 9) 1936.

In this group there were 47 deaths, giving a mortality rate of 4.7 per cent.

Sex.—The difference in the mortality rates for the two sexes was negligible, although the disease was more prevalent in males.

Age.—The condition was most common in persons in the second and third decades of life (57 per cent). Fortunately, the mortality from the disease in these persons was lowest (2 per cent). The death rate in those who were under 5 years of age was relatively high (8 per cent). Seventy-four per cent of all the patients under 5 years of age showed free pus at the time of operation.

Duration.—In 84 cases of acute appendicitis, in 5 of which peritonitis had developed, operation was performed within ten hours after the onset of the symptoms, without a single death. In cases in which operation was performed after this relatively safe period, the mortality rate increased steadily, reaching a peak (13.9 per cent) in those cases in which operation was delayed until the fourth and fifth days after the onset of symptoms. In cases in which operations were done after this period, the mortality rate shows a slight but definite drop. The death rate for the fourth and fifth days indicates without doubt that at this period the cases are "too late for early surgery and too early for late surgery." Forty-eight per cent of all the patients who gave a history of catharsis had ruptured appendixes at operation. Fifteen per cent of all the deaths occurred in patients who took cathartics.

The percentage of patients who had had previous attacks was 23.4, of patients with perforative appendicitis 15 and of patients who died 10.6. Throughout this entire series ether was the anesthetic of choice. Gas-oxygen anesthesia and local anesthesia were used if patients were gravely ill at the time of operation. In 486 cases drainage was instituted; 43 of the deaths occurred in this group. The death rate in cases of acute appendicitis in which the appendix was not ruptured was 1.5 per cent.

GENGENBACH, Denver.

ACUTE APPENDICITIS IN INFANTS AND CHILDREN UNDER FIVE YEARS OF AGE. J. H. HEYL, New York State J. Med. **36**:332 (March 1) 1936.

This article contains a good review of the problems of diagnosis and surgical treatment of appendicitis in children. Heyl believes that appendectomy is now attempted by too many inexperienced surgeons and that this is one of the factors in the increase in mortality.

AIKMAN, Rochester, N. Y.

SOME OESOPHAGEAL AFFECTIONS IN YOUNG CHILDREN. A. B. KELLY, J. Laryng. & Otol. **51**:78 (Feb.) 1936.

The cases of esophageal disease in infants and young children of which Brown Kelly speaks were observed neither in his hospital experience nor in his private practice but in the Royal Hospital for Sick Children, Glasgow, Scotland. Such cases are rarely met with in large general hospitals or in special hospitals for patients with diseases of the throat, and yet an appreciable number have been recognized by the physicians of a children's hospital within a few years.

One reason why children with congenital abnormalities or disease producing esophageal obstruction are likely to be seen rarely except in children's clinics and in general practice is that the symptoms are not characteristic. The most outstanding is regurgitation, which is commonly described as vomiting and is usually treated as such. Efforts to remedy this disturbance generally include changes in diet and various therapeutic measures, all of which involve delay. Certainly an esophageal cause of vomiting is uncommon, and one is scarcely culpable for its nonrecognition, as the relation does not suggest itself until a roentgen examination reveals the obstruction. But, before the roentgenologist is called in, death may readily occur from malnutrition or from intercurrent disease, an issue which in some instances might have been averted by the passing of a bougie. In nearly all the cases discussed the patients suffered from regurgitation. In several the onset was during the first feeding, and this at once raised the question of a congenital disturbance; in others the obstruction was less marked and caused no trouble until a semisolid diet was given.

When the obstruction is located at a high level, e. g., in atresia, only a small quantity of food can be swallowed without exciting regurgitation and coughing. On the other hand, when the obstruction is at the lower end, as in cardiospasm, and great dilatation has taken place, a large quantity of food may collect in the distended viscus before being returned. In most cases the condition comes between these two extremes. The child may take from 1 to 2 ounces (29.5 to 59 cc.) of food, then pause for a moment, and without any visible effort quietly eject the greater part of it. Quite unconcernedly he swallows more and again regurgitates, and so on throughout the meal. Some of the children never get sufficient food to satisfy them; they are constantly hungry and ill tempered. As a rule they are below the average weight and height for their age.

Following these remarks the author discusses distention of the esophagus with atrophy of the walls and dilatation of the cardia. Then he gives his attention to congenital shortening of the esophagus with thoracic stomach. Further, he discusses progressive narrowing and shortening of the esophagus with hiatal hernia. After some general considerations regarding spasm, he discusses spasmodic constriction in the lower third of the esophagus with hiatal hernia, then congenital stenosis of the esophagus with recurring spasm and ascending narrowing and finally spasm of the lower end of the thoracic portion of the esophagus and of the cardiac canal. He concludes that shortening of the esophagus may be congenital or postnatal or may begin before birth and continue to develop afterward. With reference to congenital shortening of the esophagus and the associated thoracic stomach, he stresses the following points: (1) this abnormality is not so rare as was at first supposed; (2) in the early years of life the cardiac canal is liable to spasmodic closure, which causes regurgitation and wasting; (3) the closure can be overcome by passing a bougie, and operation is not needed; (4) in later childhood there is less trouble from spasm; (5) the author knows of no death which could be directly attributed to inanition caused by obstruction of the cardiac canal of a congenitally short esophagus, and (6) necropsies on adults have proved that a thoracic position of the stomach due to congenital shortening of the esophagus does not preclude the attainment of healthy old age. Postnatal shortening and narrowing of the esophagus were found in two cases, due to spasm and associated with a large hiatal hernia. A spasm of the cardiac canal and of the lower end of the thoracic portion of the esophagus gave a characteristic roentgenologic appearance in two cases. In several of the cases the shortening of the esophagus was evidently due to both antenatal and postnatal factors. The latter were mainly of the nature of an ascending fibrosis. This condition proved fatal in several instances.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

INTUSSUSCEPTION IN TWO INFANTS: CHRONIC INTUSSUSCEPTION IN ONE; RUPTURE OF THE INTESTINE BY A BARIUM SULFATE ENEMA IN THE OTHER. M. FÈVRE, Bull. Soc. de pédiat. de Paris **34**:202 (March) 1936.

1. A boy 6 months old vomited and had diarrhea, with blood in the stool on a few occasions, for six weeks, due to chronic intussusception with partial obstruc-

tion, which finally became complete. Operation was performed, and cecocolic intussusception was found and reduced, after which the infant seemed to be doing well for a time but died several days later.

2. A boy 6 months old was admitted to the hospital on the third day after the onset of intussusception. A barium sulfate enema at a pressure of 1 meter was given under fluoroscopic observation; the fluid was seen to enter the transverse colon just beyond the head of the intussusception and without unduely distending the bowel pour suddenly into the entire abdominal cavity. Operation was done immediately, and a rent in the right part of the transverse colon, about 7 cm. long, was found, extending just out of the tumor on to the disinvaginated bowel, which was edematous but not gangrenous. Resection and anastomosis were done, and a drain inserted through Douglas' pouch, but the infant died a few hours later.

The obvious importance of early diagnosis in cases of intussusception is stressed, and the possible danger of attempts at reduction by giving a barium sulfate enema is mentioned, although this is a routine procedure in the author's practice and is followed by immediate surgical intervention if reduction does not occur.

BENJAMIN, Montreal, Canada.

MEGA-ESOPHAGUS. J. M. ROJAS and M. M. ROJAS, Rev. med. latino-am. **31**: 693 (March) 1936.

A case of greatly dilated esophagus in a woman aged 33 is reported. The symptoms, first observed when she was 12, were dyspnea, dysphagia, a sensation of food being caught in the chest, a sensation of pressure in the chest, increased fremitus and bronchophony.

DWYER, Kansas City, Mo.

CHRONIC CONSTIPATION AS A CAUSE OF INCONTINENTIA ALVI. R. PRIESEL and J. SIEGL, Arch. f. Kinderh. **107**:133, 1936.

As a result of chronic constipation and the pressure of the accumulated fecal mass, small portions of stool, often thin and mixed with mucus, may be passed almost continuously. The child becomes accustomed to the constant soiling, and incontinence becomes a habit.

CRANE, Chicago.

FURTHER OBSERVATIONS ON APHTHOUS STOMATITIS. W. HERTZ, München. med. Wchnschr. **83**:516 (March 27) 1936.

Hertz adds to his previous observations (1935, in 1,438 subjects) on aphthous stomatitis. He found no attenuation of the virus in lesions which had been treated with antiseptic solutions. The acquired immunity of guinea-pigs after vaccination with the stomatitic virus lasts a maximum of ten months. Twice measles was observed to shorten the course of aphthous stomatitis.

BRAHDY, Mount Vernon, N. Y.

EFFECT OF SLEEP OF THE GASTRIC FUNCTION OF CHILDREN. L. G. EPSHTEYN and A. S. PIPKO, Vrach. delo **19**:67, 1936.

The authors report their observations on the effect of sleep on the emptying time of the stomach.

The material consisted of fifteen children of the preschool age (from 3 to 6 years) arranged in three groups of five children each. The first two groups received an "ordinary" feeding, consisting of 200 Gm. of cream of wheat and 5 Gm. of butter, while the third group received a feeding high in fat, consisting of 20 Gm. of cream of wheat and 15 Gm. of butter. Barium sulfate was added to the cream of wheat, and roentgenologic observations were made repeatedly, on different occasions, on all the children, after periods of sleep as well as after periods of wakefulness.

In all of the fifteen subjects of the experiment it was observed that sleep definitely accelerates the emptying time of the stomach. This was particularly well demonstrated in the group of children on the diet high in fat, which per se greatly slowed up the emptying time of the stomach. In this group the maximum difference between the emptying time for sleep and that for wakefulness was as much as one hour and fifty minutes.

The authors believe that the accelerating action of sleep on the emptying time of the stomach can be explained by an increase in peristalsis and a relaxation of the pylorus.

BODER, Los Angeles.

DECOMPRESSION OF THE GASTRO-INTESTINAL TRACT: I. THE USE OF CERTAIN SIMPLE MECHANICAL APPLIANCES FOR THE CONTROL OF ABDOMINAL DISTENTION. H. H. LOUCKS and H. C. FANG, Chinese M. J. **50**:97 (Feb.) 1936.

This article comes from the department of surgery of the Peiping Union Medical College. It does not deal specifically with the decompression of the gastro-intestinal tract in children. The authors use the duodenal tube in lavage of the stomach and duodenum and recommend the continuous intravenous drip to supply abundant fluids after the decompression of the intestinal tract.

NEFF, Kansas City, Mo.

A CASE OF INTESTINAL INFANTILISM. A. J. C. HAEX, Maandschr. v. kindergeneesk. **5**:174 (Jan.) 1936.

At autopsy on a boy of 1 year cirrhotic pancreatitis was found. The question whether the changes in the pancreas were primary or secondary is discussed. As regards the etiologic background, Haex accepts the theory that the disease is due to a primary disturbance in the function of the intestines, especially to decreased resorption of fatty acids.

VAN CREVELD, Amsterdam, Netherlands.

MEGACOLON CONGENITUM TREATED WITH LUMBAR SYMPATHECTOMY. A. ODELBERG, Nord. med. tidskr. **11**:178 (Jan. 31) 1936.

A boy aged 9 had typical symptoms of congenital dilatation of the colon. He was treated by laparotomy and extirpation of the sympathetic trunk from the second to the fourth lumbar ganglion. One week after operation the stools were spontaneous. At reexamination six months later it was found that the bowels moved daily without clysma or aperients. Roentgen examination of the colon gave identical results before and after operation.

WALLGREN, Gothenburg, Sweden.

Nervous Diseases

THE KAYSER-FLEISCHER RING IN WILSON'S DISEASE AND MICROCEPHALY. L. BOTHMAN and D. E. ROLF, Am. J. Ophth. **19**:26 (Jan.) 1936.

Bothman and Rolf describe Wilson's disease, review the literature on it, and discuss the symptoms, pathologic changes and associated phenomena. They report four cases and make the following comments and conclusions:

"*Comments.*—The occurrence of the Kayser-Fleischer ring is not so rare as has been commonly believed, for the four cases here recorded were seen within a period of nine months.

"In the classical description of Wilson's disease, there is involvement of the liver, yet in the three unquestioned cases of this condition here recorded none showed either an enlarged liver or disturbed liver function. This is in accordance with most of the cases now on record in the literature. In the fourth case also, the liver was of normal size.

"Case 2 is of unusual interest because of the presence of the Kayser-Fleischer ring in a child showing microcephaly but as yet not evidence of extrapyramidal disease. The patient is only eight years old and may still develop a true Wilson's symptom complex. Her brother (case 1) began to develop symptoms at 15½ years of age. In no previous report has the Kayser-Fleischer ring been described in so young an individual. Its presence at this age may indicate that it does occur early and escapes notice until after the pronounced extrapyramidal signs lead to a diagnosis of lenticular degeneration.

"*Conclusions.*—1. Three fairly typical cases of lenticular degeneration with Kayser-Fleischer ring are described.

"2. Signs of pyramidal disease and microcephaly together with a typical Kayser-Fleischer ring are described as occurring in the younger sister of one of the patients with true Wilson's disease."

REESE, Philadelphia. [ARCH. OPHTH.]

AN ANENCEPHALIC MONSTER WITH "RHINODYMIE" AND OTHER ANOMALIES. S. B. BRODER, Am. J. PATH. **11**:761 (Sept.) 1935.

The article should be consulted for details. There are excellent reviews of the literature and a discussion of the mechanism of rhinodymia.

MOORE, New York.

THE BRAINS OF INFANTS AND CHILDREN IN RELATION TO POSTMORTEM TIME, TOXICITY AND CONVULSIVE STATE. C. R. TUTHILL, Am. J. Path. **12**:269 (March) 1936.

The brains of thirty-four infants and young children who died of acute infections, second degree burns, allergy and lead poisoning did not show changes in the ganglion cells that could be attributed to toxicity. The loss of cytoplasm, the density of the staining of the cytoplasm, the tingeing of the nerve tissue and the hyperchromatism of the nuclei and perivascular spaces varied somewhat with the age and with the fixative but chiefly with the time elapsed post mortem. The indications of toxic injury were found rather in the reactions of the microglia and macroglia. The most severe and most frequent lesions in the brains were those produced by the vascular disturbances in the convulsive states that accompany many diseases of infancy and early childhood.

MOORE, New York. [FROM THE AUTHOR'S SUMMARY.]

DUPLICATION OF THE SPINAL CORD WITH SPINA BIFIDA AND SYRINGOMYELIA. A. WEIL and W. B. MATTHEWS, Arch. Path. **20**:882 (Dec.) 1935.

This report concerns one of the rare instances of duplication of the lower segments of the spinal cord. The case may be classified with the relatively few instances of duplication of the spinal cord due either to lack of closure of the open neural tube and folding of its lateral walls or to lack of fusion of the two separated tubes of the solid anlage of the lumbar segments into one central canal.

The case reported is of interest on account of the manifold evidences of retardation of development. There was an unusual preservation of ciliated ependymal cells and supportive spongioblasts in a child aged 5 months. The mitotic figures in the nuclei of the foci of proliferated glia cells indicated that the embryonic tendency to growth had not yet been arrested or led into adult channels.

The formation of a central cavity of necrosis within the foci of glial proliferation in the upper dorsal segments sheds an interesting light on the development of syringomyelia. It supports the prevalent theory that syringomyelia arises from central necrosis of an intramedullary gliobastoma. The presence of mitotic figures and the active proliferation of glia cells with the formation of primitive spongio-

blasts indicate that in this case a neoblastic formation was present, a glioblastoma, and not merely a reactive gliosis stimulated by the pressure atrophy of the spinal cord following marked hydromyelia.

Another interesting feature is the development of the anterior and posterior horns of gray matter and their corresponding nerve roots in the duplicated segments. Though there were two anterior horns in each half, only the more anteriorly situated contained well developed neurons and gave rise to an anterior root. From the second, underdeveloped anterior horn of gray matter no axons streamed peripherally. In some sections there was the suggestion of two posterior horns in each half, but the one situated more posteriorly usually was atrophic. In most sections the two horns were combined, and only one posterior root arose near the middle of the lateral surface of the cord. These observations are of considerable interest to the embryologist. They testify to the development of spinal nerve roots and muscle metameres independent of the development of the spinal cord. In this connection may be cited the case reported by Sokolansky, who described absence of the spinal cord in a fetus in the presence of well formed posterior spinal nerve roots and ganglions. In the present case, furthermore, only one well formed column of Clarke was present in each half of the duplicated cord. It was situated on the side of exit of the posterior nerve root, i. e., in the anterior half of each duplication. The intersegmental nerve connections of each half of the spinal cord were well developed. There were an anterior and a posterior commissure containing myelinated fibers, and the intersegmental fiber tracts were well formed. Except for a rather wide zone of marginal glia, there was no abnormality in the formation of the posterior, lateral and anterior columns, which contained numerous myelinated fibers.

Many theories have been advanced to explain such a duplication of the spinal cord associated with rachischisis. Most former investigators assumed that the whole spinal cord arises from an open neural tube and concluded, therefore, that failure of the tube to close resulted in the duplication. More recently Holmdahl, Ikeda and others suggested that early in embryonic life the caudal part of the spinal cord develops not from an open tube but from a solid bundle of cells, in which two or more cavities are formed. Later, the two tubes become confluent, and the united cavities form the central canal. Failure of such a fusion results in persistent duplication of the lower segments of the spinal cord; around each cavity nerve tissue forms a spinal cord, which is separated from its duplicate by ingrowing connective tissue.

WINKELMAN, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

MENINGITIS IN MAN CAUSED BY A FILTERABLE VIRUS: TWO CASES AND THE METHOD OF OBTAINING THE VIRUS FROM THEIR SPINAL FLUIDS. T. F. M. SCOTT and T. M. RIVERS, J. Exper. Med. **63**:397 (March) 1936.

The clinical pictures presented by two men suffering from acute bacteria-free lymphocytic meningitis and the method by which the causative virus was obtained from their spinal fluid are described. Evidence is then adduced to show that the virus was really in the spinal fluids and that the two strains obtained from the two patients were identical or closely related and etiologically significant.

Most of the spontaneous virus diseases of the human central nervous system that have been described in the past seem to have attacked primarily the substance of the brain and spinal cord and to have involved the meninges, if at all, secondarily. In the present cases, the history and clinical findings point to the fact that the main part, if not all, of the insult to the central nervous system was borne by the meninges.

This paper is of particular interest because only on rare occasions has a virus been isolated from the spinal fluid. KNICKERBOCKER, Dallas, Texas.

TERATOMA OF THE SPINAL CORD. P. C. BUCY and D. N. BUCHANAN, Surg., Gynec. & Obst. **60**:1137, 1935.

The tumor first caused symptoms at the age of 16 months but was not removed until the child was almost 3 years old and suffering from mixed and alternating spastic and flaccid paraplegia. The tumor was cystic, contained 35 cc. of glairy material, showed a mural nodule and lay within the arachnoid. In common with the ten previously recorded examples of teratoma of the cord, the growth contained ectodermal and mesmodermal but no entodermal derivatives. The origin was traced to the posterior columns at the caudal end of the cord.

HUNTER, Portland, Ore. [ARCH. PATH.]

FAMILIAL DEGENERATION OF THE CEREBELLUM IN ASSOCIATION WITH EPILEPSY. FREDERICK THORPE, Brain **58**:97, 1935.

Thorpe describes the cases of two brothers with epilepsy and a well marked cerebellar symptom complex. One died of phthisis and presented an opportunity for study of the central nervous system, which revealed pure cortical cerebellar atrophy. As far as Thorpe could determine from a review of the literature, this is the first case of familial degeneration in which the atrophy was limited to the cortex.

The important features of the family history were excessive alcoholism on the paternal side and tuberculosis on the maternal. No member of a family of twelve children suffered from epilepsy except the two brothers to be described. In the first case epileptic seizures began at the age of 3 years, and at 25 psychotic symptoms necessitated admission to a hospital for patients with mental diseases, where the patient remained until death, at the age of 46. At the age of 38 he had an attack of typhoid. At the age of 41 he showed cerebellar ataxia, involving all limbs. The ataxia gradually increased until the patient's death from pulmonary tuberculosis. The second patient presented the first epileptic seizure at the age of 19 years, and at the age of 33 mental symptoms necessitated admission to a hospital for patients with mental diseases, where he improved and was released after a few months. The mental symptoms returned, and he was readmitted at the age of 40. At the age of 37 he began to become unsteady on his feet, and at 40 he had a markedly ataxic gait. Neurologic examination revealed a well marked cerebellar symptom complex. Additional features of interest in this case consisted of static tremors of the head and limbs, hypertonia during movement and hypometria of the upper limbs, producing a typical *freinage* reaction (bradyteleokinesis).

Autopsy in case 1 revealed an advanced stage of chronic ulcerative phthisis involving the upper lobe of the left lung. The cerebellum was smaller than normal and was markedly atrophied. The weight of the cerebellum and brain stem was 130 Gm., instead of the normal 170 Gm. The atrophy was more marked on the anterior and superior surfaces, particularly in the superior part of the vermis and the semilunar and quadrilateral lobules. Histologic studies of these areas showed almost complete destruction of the Purkinje cells, marked narrowing of the molecular layer and thinning of the granular layer. The outer third of the molecular layer showed status spongiosus, while the granular layer showed marked rarefaction. The inferior surface of the cerebellum showed a less severe involvement of the cortex, the main incidence of the disease appearing to fall on the Purkinje layer, with the molecular and granular layers presenting an almost normal appearance. The basket cells were little affected. In sections from the upper surface of the cerebellum the axons of the few remaining Purkinje cells presented a large fusiform swelling, situated a short distance from the base of the cell, and in the outer third of the granular layer were the *Axonschwellungen* described by Bouman.

The dorsal region of the spinal cord was abnormally slender and presented a peculiar ribbed appearance, due to deepening of the posterolateral grooves. Histologically, except for deepening of the posterolateral groove on one side, the cord was normal.

This case corresponds to the sporadic cases of primary parenchymatous degeneration of the cerebellar cortex, the number of which at present is limited to twelve. These cases were all of nonfamilial type. Review of the literature failed to disclose any case of familial type in which the lesion was confined to the cerebellar cortex. Holmes (1907) described four cases of cerebellar degeneration in one family. Pathologic study of one of them revealed, in addition to a typical cortical involvement, sclerosis of the inferior olives; as a result of this observation the case has been classed as an instance of olivocerebellar atrophy. All four of Holmes' cases were similar to those described by Thorpe, who believes that there is little justification for placing them in a separate group.

The familial form of degeneration of the cerebellum differs from the sporadic only in the tendency to appear at an earlier age. When Holmes' four cases of the familial form are included, the average age of onset is 37 years, whereas that of the sporadic form is 62 years. The clinical manifestations are essentially similar in the whole group of cases, viz., gradual and insidious onset of muscular incoordination, involving the body symmetrically and progressing steadily and slowly over a number of years to helplessness and death from intercurrent disease. In the majority of cases the lower limbs are affected before the upper, and speech becomes monotonous and drawling. Nystagmus is unusual, and hypotonia is rarely prominent.

In these cases there appears to be an inherited endogenous tendency toward early degeneration or abiotrophy of the cerebellar system of neurons. Cerebellar atrophy may be inherited as a mendelian recessive character, in a manner similar to that in Friedreich's disease. The close association between cerebellar atrophy and Friedreich's disease is borne out by the presence of a slender and asymmetrical cord in the first patient. Similar development defects are not infrequent in Friedreich's disease.

Epileptic seizures were present in both Thorpe's cases. Spielmeyer (1930) observed characteristic cell degeneration in the cornu ammonis and cerebellum in 80 per cent of the brains of subjects with epilepsy. However, these changes consisted of focal areas of atrophy and sclerosis, whereas in the group of primary degenerations of the cerebellum, of which the case described is a typical example, the cerebellar lesion is widespread, diffuse and symmetrical atrophy. The association of cerebellar atrophy and epilepsy in these two cases is regarded as accidental and merely represents the not uncommon occurrence of a predisposition to two independent nervous disorders in one person.

SALL, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

LYMPHOCYTIC MENINGITIS WITH RECOVERY. MICHAEL CAMNER and MARIE CAMNER, Bull. Soc. de pédiat. de Iasi **6**:47 (April-June) 1935.

The case under consideration was that of a boy 9 years of age who before admission to the hospital had suffered from general malaise, fever and vomiting for six days. On the fourth day in the hospital the neck was stiff, and lumbar puncture yielded a fluid with 110 lymphocytes per cubic millimeter, a positive Pandy reaction and a positive Nonne-Appelt reaction. These findings were noted on several subsequent lumbar punctures. No tubercle bacilli were found. Recovery was complete two weeks later.

The authors feel that recognition of cases of this type is necessary in order to prevent an erroneous diagnosis of tuberculous meningitis.

LESLIE, Evanston, Ill.

FRIEDREICH'S DISEASE ASSOCIATED WITH CONGENITAL SYPHILIS. L. BABONNEIX and ROUÈCHE, Bull. Soc. de pédiat. de Paris **34**:154 (March) 1936.

A girl 15 years old had some signs of Friedreich's ataxia, which had made their appearance three years previously. Some of the features typical of the disease were not present. The Wassermann reaction of the blood was negative, but the mother and grandmother were afflicted with tabes and dementia paralytica, respectively. The girl later presented paronychia of the great toe, which was considered to be syphilitic. There was nothing suggestive of Friedreich's ataxia in any other members of the family.

BENJAMIN, Montreal, Canada.

A CASE OF PERICRANIAL SINUS. M. FÈVRE, Bull. Soc. de pédiat. de Paris **34**: 190 (March) 1936.

A boy 10 years old had a fluctuating, pulsating round flat swelling in the left frontal region. It was noticed first when he was 7 years old. The fluid could be expressed. The first recorded instance of a condition such as this was that described as pericranial sinus by Stromeyer in 1850. The sac communicates with the longitudinal sinus, and its location is frontal or occipital. The operative treatment consists in extirpation of the sac and obliteration of the opening in the skull, through which the connecting vein passes, with wax. This procedure was adopted in Fèvre's case, and two years later the boy was well and the condition had not recurred. The etiologic background is congenital, but trauma has also been mentioned as a contributing cause.

BENJAMIN, Montreal, Canada.

PROGNOSIS OF CONVULSIONS IN INFANCY AND CHILDHOOD. N. FAXÉN, Rev. franç. de pédiat. **11**:665, 1935.

The findings presented in this study are based on observation of 396 children admitted to the Children's Hospital of Gothenburg during the period of 1922 to 1931 for loss of consciousness or convulsions. Among the convulsions of organic origin those due to malformation and obstetric trauma have a particularly serious outlook. The children who had nonspecific encephalitis recovered entirely. Of 95 children with epilepsy, 15 became symptom free, 36 showed inferior mental development, and 7 died. In 41 children in whom the origin was thought to be psychogenic no epilepsy developed. Among 238 children with convulsions associated with infectious diseases, 4 showed signs of mental retardation at the first examination, 6 presented this stigma later, 12 became epileptic, and 15 died. Poor heredity and pathologic delivery were encountered more frequently in the histories of epileptic patients than in those of children with accidental convulsions (psychogenic or associated with infectious diseases).

The age of the first attack is most often below 4 years in those with epilepsy and in those with accidental convulsion. However, accidental convulsions rarely occur after the fourth year. Epileptic convulsions tend to be spaced at regular intervals, while accidental convulsions in more than half of the cases occur throughout only a brief period of time. This study does not include convulsions due to spasmophilia.

LESLIE, Evanston, Ill.

IMPORTANCE OF THE SIGN OF VESTIBULAR DISHARMONY IN A CASE OF ABSCESS OF THE CEREBELLUM. L. LEVESQUE, F. BARRON and A. CHARBONNEL, Rev. d'oto-neuro-opht. **13**:186 (March) 1935.

The case reported was that of a child aged 5 years who during convalescence from bilateral mastoidectomy after an attack of scarlatina suddenly experienced fever, occipital headache and hyperextension of the neck. Associated with these symptoms was a disharmonious vestibular syndrome, consisting of nystagmus to the diseased side, deviation of the arms, Romberg's sign and lateropulsion in the same direction as the nystagmus; there was a slight but distinct cerebellar dysmetria, which of itself was not sufficient evidence on which to base a diagnosis of

abscess of the cerebellum. On account of these two syndromes immediate exploration of the cerebellum was made, and an abscess was evacuated. Later, the deviation of the arms and the Romberg sign were changed in direction. Death occurred suddenly two months after intervention, from an undetermined cause. The association of the disharmonious vestibular syndrome was the deciding factor in the diagnosis. DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

ANATOMICOCLINICAL SYNDROME OF TUMOR OF THE FOURTH VENTRICLE FROM THE OTONEUROLOGIC POINT OF VIEW. G. S. ZIMMERMANN and A. S. TCHERNYSCHEW, Rev. d'oto-neuro-opht. **14**:29 (Jan.) 1936.

A tumor of the fourth ventricle is manifested by local and remote symptoms, the latter by effect of the enormous hydrocephalus. Of the local symptoms, pathologic phenomena of the eighth nerve occupy first place; disturbances of the cochlear division are more rare than those of the vestibular. The clinical and anatomicopathologic aspects depend on the stage of evolution at the time of examination.

The case reported is that of a boy aged 14 years. His symptoms had begun two years before with headaches, followed by attacks of vertigo. Ten weeks before death he became blind, owing to atrophy of the optic nerve following papillary stasis. Good hearing with shortened bone conduction, spontaneous deviation inward of the arms and a Romberg sign (falling backward) were observed. Postrotatory horizontal nystagmus of large amplitude toward each side and inverse past pointing were elicited. Tests for falling and past pointing after douching gave normal results. No localizing diagnosis was made. At autopsy a tumor was noted on the ventral surface of the brain, between the cerebellum and the medulla. The tumor (perithelioma) compressed the right tonsil of the cerebellum and the median parts of the biventer and gracilis lobes on both sides and filled the fourth ventricle, compressing the dorsal part of the pons, the tonsils and the tuber vermis. Microscopic examination of serial sections revealed no degeneration of the ventral and dorsal cochlear nuclei. The cells of the nuclei of Deiters, Bechterew and Schwalbe were degenerated, and the glia was proliferated. Degenerative changes were present also in the nucleus of Roller bilaterally, the fibers of the nucleocerebellar tract, the cells of Purkinje, the lingual and central lobes, the pyramid, uvula, nodulus and biventer and gracilis lobes and all the central cerebellar nuclei. The indemnity of the cochlear nuclei is explained by the fact that they are situated more deeply in the floor of the ventricle than the vestibular nuclei. The spontaneous inward deviation, the inverse deviation after stimulation and the nystagmus of wide amplitude were caused by disturbances of function of the nucleocerebellar fibers, the function of which is inhibitory. From the fact that correct falling occurred in the caloric test in the presence of the alterations observed, the authors conclude that: (1) the pathway of the falling reaction does not necessarily pass by way of the vermis and (2) the static disturbances (falling backward and staggering gait), associated with a correct falling reaction to stimulation of the labyrinth, are due exclusively to changes in the vermis. DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

NONSUPPURATIVE OTOGENOUS ENCEPHALITIS OF THE TEMPORAL REGION. J. A. BIJLEVELD, Rev. d'oto-neuro-opht. **14**:81 (Feb.) 1936.

Nonsuppurative otogenous encephalitis is almost always diffuse. The patient has continuous high fever, without slowing of the pulse, and headache, which is less characteristic than that due to cerebral abscess. Bijleveld reports the case of a child aged 5 years whose symptoms were different from those characterizing the classic form of the disease. After bilateral mastoidectomy the fever was of the pyemic type; the pulse was very rapid; cultures of the blood were sterile; meningeal reaction was not present, and there were marked focal signs (mimic facial paralysis on the left side). The right temporal lobe was explored with negative results so far as the presence of pus was concerned, but softened cerebral

tissue was aspirated through the exploring needle. Since there was no improvement in the condition of the patient, radical mastoidectomy was performed, and the patient made a prompt and complete recovery.

Nonsuppurative otogenous encephalitis is probably more frequent than is suspected. A focus of osteitis somewhere is indispensable for the production of encephalitic infection, and one can never be sure that otitis media is completely cured. Therefore, in a case of otogenous encephalitis or of cerebral abscess, if improvement is not prompt after simple mastoidectomy or if, after ample drainage of the abscess, it tends to extend and the patient is not apyretic in a few days, radical mastoidectomy should be done at once.

DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

MENINGEAL AND ENCEPHALIC REACTIONS TO OPERATIONS ON ENCEPHALITIC ABSCESSES. E. Bozzi, Arch. ital. di otol. **47**:679 (Oct.) 1935.

Bozzi made experiments in rabbits in order to clarify some of the points related to (1) the selection of the operation for a cerebral or a cerebellar abscess, which depends on the type of dural incision (small or large), and (2) the part that meningeal adhesions play in producing encephalitic reactions. He found that the application of iodine to the dura for forty-eight hours is harmless both to the meninges and to the encephalon and does not cause adhesions between the meningeal layers, though it causes slight meningeal reactions. He studied the several stages of the evolution of the operation performed according to Lemaitre's technic. Applying iodine to the dura before it is opened does not offer any advantages over the technic commonly used. When Lemaitre's technic is used local meningitis, the focus of which is in contact with the drainage tubes, develops within six hours after the operation. Connective tissues begin to grow within twenty-four hours, which within eight days form a complete tampon that prevents dissemination of the localized meningitis. Lemaître's technic does not harm the encephalon. Experiments with a large meningeal incision gave poor results. Such experiments turned out better, however, when iodine was applied to the dura before the incision was made. Bozzi says that only the results in a large clinical series will solve the problem of selecting the operation. Lemaître's technic seems to be indicated in a large number of cases, although in general an eclectic stand is advisable.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

ROENTGEN THERAPY IN HYDROCEPHALUS. E. VON LEDERER, Arch. f. Kinderh. **106**: 31, 1935.

Roentgen radiation promises good results in hydrocephalus in those cases in which the excess of fluid is a result of overproduction, while the probability of recovery is less favorable in cases in which a decrease in resorption or an obstruction is present. In poliomyelitis, roentgen therapy often is followed by results, which cannot, however, always be evaluated as results of the roentgen treatment. Roentgen radiation offers no results in feeblemindedness.

CRANE, Chicago. [FROM THE AUTHOR'S SUMMARY].

MULTIPLE CONGLOMERATE TUBERCLES OF THE BRAIN IN A CHILD. P. KISS and I. FÉNYES, Arch. f. Kinderh. **107**:77, 1936.

A case is reported.

CRANE, Chicago.

INJECTION OF AIR INTO CYSTIC TUMORS OF THE BRAIN IN CHILDHOOD. P. KISS and I. FÉNYES, Arch. f. Kinderh. **107**:129, 1936.

In diagnostic puncture of a cystic tumor of the brain, after removal of the fluid an equal volume of air is injected. This acts as a tampon to prevent bleeding and aids in localization of the tumor by roentgenologic examination.

CRANE, Chicago.

PROLONGED LATENCY OF OTOGENIC ABSCESS OF TEMPORAL LOBE WITH RARE HISTOLOGIC ASPECTS. B. KECHT, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **140**:261, 1936.

Kecht describes a large otogenic abscess of the left temporal lobe in a child aged 11. The case is worthy of attention, particularly on account of the prolonged latency, for the abscess perforated ten months after otitis media, which had lasted for about two weeks. Other unusual aspects were a deficiency of symptoms, a rare mode of transition of the causal suppuration of the middle ear —by way of dehiscence of the bones—and a rare type of membrane formation and of abscess growth.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

A TUMOR OF THE OPTIC NERVE. K. SCHWARZ, Arch. f. Ophth. **135**:247 (March) 1936.

Schwarz reports the case of a girl 3½ years of age in whom unilateral exophthalmos, amaurosis, papilledema and dilatation of the optic foramen had gradually developed. Certain parts of the choked disk looked strikingly solid and gray. The other eye was normal. Exploration of the orbit through an incision made in the eyebrow revealed a spindle-shaped tumor surrounding the whole orbital portion of the optic nerve. Because the parents would not permit enucleation, most of the tumor was excised. Anatomic examination revealed that it extended in both directions beyond the limits of the removed portion. Foerster, of Breslau, Gremany, recommended removal of the intracranial portion of the nerve by the transfrontal route. The parents, however, agreed only to enucleation. During the course of this, a part of the intracanalicular portion of the nerve was also removed. In the following year radium in six doses, 40 milligram hours each, was applied through the conjunctiva in the direction of the optic foramen. At the time of publication, viz., six years later, the patient was in good health and showed no signs of local recurrence. The other eye was perfectly normal.

The histologic picture was that of endothelioma plus a considerable amount of connective tissue proliferation, which the author calls fibromatosis. The tumor had a malignant character, for in the region of the papilla it exhibited infiltrative growth.

KRONFELD, Pieping, China. [ARCH. OPHTH.]

HUNTINGTON'S CHOREA IN A FAMILY GROUP. K. WASUM, Arch. f. Psychiat. **103**:78 (Feb.) 1935.

Wasum studied cases of Huntington's chorea in which he was able to determine the presence of this disease in five generations. Seventy-six members of the family were included in this study. The chorea was of the pure Huntington type. It was found that the chorea was transmitted in a direct line, so that the descendants of persons who did not have chorea were free from the disease. There was a tendency for anteposition of the onset of the disease so that from generation to generation the onset occurred at a progressively earlier age. In all the patients the disease began with psychic disturbances, such as outbursts of anger, jealousy and irritability. Following these there developed the first signs of motor disturbances, which seemed to cease during sleep in all the patients; finally there was deterioration. Neurologically, the symptoms were primarily of the extrapyramidal type. Anatomically, there were gross atrophies of the basal ganglions. The histologic picture was characterized by destruction of ganglion cells and proliferation of astrocytes and fibrous glia, with marked atrophy of the nerve fibers. These findings were particularly pronounced in the striatum.

W. MALAMUD, Iowa City. [ARCH. NEUROL. & PSYCHIAT.]

LESIONS OF THE SPINAL CORD IN RACHITIC KYPHOSCOLIOSIS. A. PONSOLD, Arch. f. Psychiat. **103**:199 (May) 1935.

Ponsold reports the case of a man aged 21 who suffered from kyphoscoliosis for ten years. During the last few weeks before admission to the hospital there

developed spastic paraparesis of the legs, accompanied by anesthesia from the seventh to the tenth dorsal segment and hypesthesia from the tenth dorsal segment to the toes. Roentgenograms showed scoliosis with the convexity to the left. Lumbar puncture and injection of iodized sesame oil showed block at the level of the eighth and ninth dorsal vertebrae. Some of the sensory disturbances apparently were produced by pressure on the dura, and the anesthesia was probably produced by traction on the roots. The part of the cord which was nearest the convexity was affected much more severely than the other side, and thus was produced an incomplete transverse lesion. Laminectomy was followed by slow and incomplete disappearance of the clinical signs.

W. MALAMUD, Iowa City. [ARCH. NEUROL. & PSYCHIAT.]

EXPERIMENTAL AND CLINICAL INVESTIGATIONS OF THE ROENTGENOGRAPHIC VISUALIZATION OF THE SURFACE OF THE BRAIN. K. KOSHIMIZU, Fortschr. a. d. Geb. d. Röntgenstrahlen **53**:25 (Jan.) 1936.

Although the results obtained with thorotrast (thorium dioxide) are far superior to those with other contrast mediums, the substance is so injurious to patients that its general use for the purposes expressed in the title of the paper cannot be recommended at the present time.

McCUNE, New York.

ROENTGEN TREATMENT OF EPILEPSY. M. SGALITZER, Fortschr. a. d. Geb. d. Röntgenstrahlen **53**:580 (March) 1936.

The following physiologic effects of roentgen irradiation of tissues make the roentgen ray of value in the treatment of epilepsy of certain types. It is effective in diminishing hydrocephalus, probably through decreasing the production of cerebrospinal fluid; it accelerates the resorption of inflammatory exudates and hemorrhages; it affects the state of tonus of the cerebral blood vessels. Sgalitzer's experience with roentgen therapy in epilepsy is as follows: Of eighteen patients with traumatic epilepsy, five were not helped, nine were improved, and four were strikingly benefited. Thirty patients with "idiopathic" or "true" epilepsy were treated; eight were not improved, sixteen received some benefit and six were conspicuously bettered. Of eight patients with epilepsy due to or associated with hydrocephalus, two were helped by treatment, and six went at least two years without a single attack. Some improvement was noted in ten patients with petit mal, although in none did the attacks cease entirely. The ray was applied directly to the skull in varying doses, which are described in detail. The author expresses the opinion that whenever epilepsy is refractory to medicinal therapy it should have a trial of roentgen therapy.

McCUNE, New York.

NEURINOMA OF THE PERIPHERAL PART OF THE FACIAL NERVE. F. ALTMANN, Monatschr. f. Ohrenh. **69**:1042, 1935.

Altmann presents a symptom complex that is caused by a tumor of the type designated as neurinoma which, in view of the localization of the growth in the region of the middle ear or in that of the external auditory meatus and in view of the clinical symptoms, seems to originate in the facial nerve. He reviews some earlier reported cases and gives the histories of several others. His summarizing comment is based on six cases. With the exception of one case, all occurred in rather young persons (aged between 16 and 26). The first symptom of the disorder is always paralysis of the facial nerve, which usually persists during the entire course of the disorder. Often this paralysis is for a long time the only clinical symptom of the disease. If the ear is examined, the auditory meatus is usually found partly or completely filled by a polypous tumor which seems to originate on the posterior wall of the external auditory meatus. The tympanic membrane, as far as it can be seen, is usually intact and remains so for a comparatively long time. The hearing is likewise normal in the beginning but later becomes impaired,

either because the growing tumor obstructs the external auditory meatus or because the tumor involves the middle ear. When the latter involvement is present, the tympanic membrane may be destroyed, and suppuration of the middle ear may develop. A correct diagnosis can be based only on an exploratory excision. If the findings are negative, the incision should be repeated, particularly if a secondary chronic suppuration with granulation tissue has developed. The growth of the tumor is usually rather slow and may even cease for several years. The growth is dangerous on account of its position near the middle ear or near the labyrinth, for these locations involve the danger of complications in the middle ear, the labyrinth or even the brain. On the basis of his therapeutic observations Altmann advises that ray therapy should be dispensed with, but that surgical treatment is advisable, particularly during the early stages, when there is still hope of counteracting or improving the facial paralysis. Regarding the prognosis he says that it is favorable as far as the life expectancy of the patient is concerned, provided, of course, severe complications are prevented, but that it is unfavorable as far as local restitution is concerned.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

GENETIC AND CLINICAL ANALYSIS OF THE TORSION SYNDROMES. J. A. BEILIN, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:126, 1935.

Two Jewish boys aged 10 years presented torsion dystonic features of the left extremities, and with the discovery of their relationship, Beilin was led to examine the familial histories. Data for six generations consisting of 104 members were collected, of whom 42 were personally examined by the author. Eighteen types of abnormality were found: epilepsy, 1 case; migraine, 1 case; spasmophilic convulsive syndrome, 9 cases; short fingers, 4 cases; anomaly of the fifth finger, 4 cases; short stature, 10 cases; tremor in various parts of the body, 4 cases; hypertrichosis of the back, 6 cases; nocturnal incontinence, 3 cases; blue scleras, 6 cases; severe concavity of the foot, 5 cases; flatfoot, 1 case; Babinski sign (pseudo-Babinski sign), 5 cases; microcephaly, 2 cases; squint, 2 cases; stuttering and stammering, 2 cases; hypoplasia (?) of the thyroid, 6 cases, and intermarriage of relatives, 1 case. The course of the torsion dystonic elements is considered as of a heterozygous recessive type without any relation to sex. Of special significance are the longevity and abundance of children, which are striking in the family. Although a clinical relationship has been postulated between athetosis and torsion dystonia, the author does not find this to be the case in heredity. Torsion dystonia must not be confused with Wilson disease or Westphal-Strümpell disease.

MICHAELS, Boston. [ARCH. NEUROL. & PSYCHIAT.]

MULTIPLE SCLEROSIS IN TWINS. M. ASTWAZATUROW, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:744 (Sept.) 1935.

Astwazaturow reports on two sets of twins. The first pair were dissimilar and did not present identical clinical conditions. There was atrophy of the optic nerve in one and none in the other, and the disability and its progression were much more marked in one than in the other. When they were first seen in 1927, one had definite disseminated sclerosis, while the other showed merely diminution of abdominal reflexes and a slight difference in the patellar reflexes. The author was disinclined at the time to make a definite diagnosis of multiple sclerosis in this second twin and warns of the importance of such minimal clinical findings, especially when there is evidence of the fully developed disease in the other member of the family.

The second pair of twins came for examination when one of them, a medical student, wished to be examined for nystagmus. He became concerned about this after hearing a lecture on the subject. Both twins showed nystagmus, diminution of abdominal reflexes and mild signs referable to the pyramidal tract. They were not sick and made no complaints. These clinical findings may be expressions of some constitutional defects for which the author suggests the term "polyscleroid

abiotrophy." While they resemble multiple sclerosis, they do not show the same tendency to progression. He is, however, not at all certain regarding the prospects of the later development of multiple sclerosis.

He also cites the case of a girl aged 15 who had mild nystagmus, hyperreflexia on the right and an Oppenheim reflex on the left. Her uncle, aged 39, also presented mild signs such as occur in multiple sclerosis (ptosis on the right, hyperactive reflexes of the upper tendon on the right, hyperactive patellar reflex on the left, mild intension tremor on the left and diminution of the abdominal reflexes on the right). The changes in these two cases were also attributed to a nonprogressive polyscleroid abiotrophic condition, though the author was uncertain regarding the future of the girl. Cases of multiple sclerosis have been reported in a daughter and father. Other members of the same family showed mild signs such as are described in the other cases.

Only two other cases of multiple sclerosis in twins have been reported (Prussak and Legras). The genetic factor in multiple sclerosis was not clear until the publication of the monograph of Curtius in 1933. The reported cases in twins confirm the probability of the importance of heredity in the genesis of multiple sclerosis.

SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

TUBERCULOMA OF THE BRAIN. I. RASDOLSKY, Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:18 (Oct.) 1935.

The reords of 13,039 autopsies from 1925 to 1934 in a hospital in Leningrad to which adults only were admitted disclosed that 32 cases of tuberculoma of the brain had been observed. Of the 32 patients, 11 entered with a syndrome of tumor, 14 with tuberculosis of the lungs and 7 with tuberculous meningitis.

In contrast with a recent opinion that the frequency of tuberculoma is decreasing, Rasdolsky noted that in Leningrad there has been no decrease in the last twenty-four years. Tuberculoma constitutes 16 per cent of all tumors disclosed at autopsies in general hospitals. In Rasdolsky's series it constituted 14 per cent. In 52 per cent of the cases in his series it caused no clinical picture of tumor but was discovered at autopsy. The incidence was much lower in neurosurgical hospitals, varying from 2 to 3 per cent. Of 146 tumors seen in the Neurosurgical Institute of Leningrad, 3 (2.1 per cent) were tuberculomas; of 8,322 patients who died of pulmonary tuberculosis and tuberculous meningitis 0.36 per cent had tuberculoma. Seven (22.6 per cent) died of the tuberculoma; 4 (13 per cent), of pulmonary tuberculosis, and 20 (64.4 per cent), of tuberculous meningitis. Tuberculoma was therefore the cause of death in only 0.08 per cent of cases in which the diagnosis at the time of admission was tuberculosis. Tuberculous meningitis, on the other hand, was the cause of death in 3 per cent of these cases.

There were 263 cases of tuberculous meningitis and tuberculoma; in 11 instances the condition was tuberculoma alone, in 21 tuberculoma and tuberculous meningitis and in 23 meningitis alone. In only 4.6 per cent of the cases involving the central nervous system was there tuberculoma without meningitis. Most (75 per cent) of the tumors were solitary; 15 were supratentorial and 9 subtentorial. Of the multiple tumors, 2 were supratentorial and 2 subtentorial; 4 were both supratentorial and subtentorial. Of the supratentorial tumors, 3 occurred in the frontal lobe, 3 in the parietal lobe, 1 in the temporal lobe, 2 in the thalamus, 1 in the caudate nucleus, 1 in the lenticular nucleus and 3 in the cerebral peduncle. Of the group of subtentorial tumors, 4 were cerebellar and 4 pontile, and 1 was in the quadrigeminal plate. These tumors occurred more often in young patients; 40.7 per cent occurred in persons in the third decade of life. The ratio of the incidence in males to that in females was 3:1. Rasdolsky asks the interesting question why tuberculoma is found so much more frequently in men than in women. He suggests that it may be due to the fact that men are more exposed to exogenous injuries, such as alcoholism, trauma to the head and perhaps infection. He assumes that all these factors in some way make the nervous system more vulnerable. He refers to cases in which tuberculoma arose a short time after trauma to the head.

Of 4 patients on whom operation was performed, 3 died immediately after the operation, and 1 lived for seven months. Removal of a deep-lying tuberculoma usually results in tuberculous meningitis. Patients do better with simple decompression. Rasdolsky, however, encourages radical removal of superficially placed tuberculomas. He collected 15 cases in which recovery followed this operation.

SAVITSKY, New York. [ARCH. NEUROL. & PSYCHIAT.]

MULTIPLE TUBERCULOMAS OF A CHILD'S BRAIN. P. KISS and I. FÉNYES, Orvosi hetil. **80**:58 (Jan. 18) 1936.

An 8 year old child was brought into the children's clinic in Budapest with the complaint of tuberculous fistulas in the neck and one foot. During the previous weeks his walking had become ataxic; he could not use his hands well and had severe headache. On the right side there were pareses of the abducens, trigeminal and facial nerves; on the left, symptoms of involvement of the pyramidal tract and sensory disturbances. Spinal fluid obtained by lumbar puncture showed a positive Pandy reaction; the protein content was increased; the number of cells was normal; the colloid gold test gave a pathologic reaction. Encephalography was carried out (by means of a ventricular puncture), and the cerebral fluid showed no pathologic alterations. The encephalography showed that the anterior horns of the ventricles were displaced to the right side. The authors thought that there were two tuberculomas: one in the pons and the other in the right frontal region. The postmortem examination justified this opinion.

GÖTTCHE, Budapest, Hungary.

THE TAKATA-ARA TEST AND ITS SIGNIFICANCE IN INFANCY AND CHILDHOOD. I. RECHT, Orvosi hetil. **80**:97 (Feb. 1) 1936.

Examination of fifty-six normal infants and twenty-six normal children showed that flocculation occurs in a dilution of 1:16. Flocculation in a stronger or weaker dilution than 1:16 signifies a pathologic situation. The details should be worked out by further examinations.

GÖTTCHE, Budapest, Hungary.

LUMBO-SACRAL MAMMIFORM TUMOUR (APPARENTLY SUPERNUMERARY BREAST) ASSOCIATED WITH SPINA BIFIDA OCCULTA. Y. T. HSIAO and P. L. LI, Chinese M. J., supp. 1, February 1936, p. 131.

Hsiao and Li report the case of a Chinese girl aged 18 years in whom there had been noticed at birth a small elevation representing a supernumerary breast. The mother tried to tie off the supposed nipple with a string, but the procedure failed because of the pain. Another congenital malformation in the child was occult spina bifida, which proved at operation to be a fatty tumor connecting with the inside of the spinal canal. This operation was done when the girl was 18 years of age.

The writers discuss the morphologic characteristics and behavior of the supernumerary breast, which grew simultaneously with the other breasts in the development occurring at puberty.

NEFF, Kansas City, Mo.

RELATIONSHIP BETWEEN INFANTILE TETANY AND SUBSEQUENT DEVELOPMENT OF EPILEPSY. V. HENDRIKSEN, Acta psychiat. et neurol. **10**:259, 1935.

In 91 per cent of cases at a large institution for patients with epilepsy, the onset of epilepsy occurred before the age of 20 years. Hendriksen investigated the incidence of epilepsy in ninety-seven infants treated for tetany in 1912 and 1913. The investigation was carried out in 1925 and 1926 and was repeated on the same material in 1932 and 1933, when the subjects had reached the age of 20 or over. At the time of the last investigation seven patients had died of tetany in infancy, and ten had died between 2 and 16 years of age. Of the latter, epilepsy had

developed in only two; these two patients, however, were also mentally defective. The fate of twenty-nine patients was unknown. None of them had been admitted to the only colony for persons with epilepsy in the state (Denmark). Of the fifty-one remaining persons who were known and living at the time of the investigation, none suffered from epilepsy. Hendriksen concludes that infantile tetany does not lead to epilepsy later in life.

YAKOVLEV, Palmer, Mass. [ARCH. NEUROL. & PSYCHIAT.]

ANATOMICOPATHOLOGIC SUBSTRATUM OF TORSION DYSTONIA. C. J. MUNCH-PETERSEN, Acta psychiat. et neurol. **10**:391, 1935.

Munch-Petersen reports the case of a boy aged 18 years, of healthy stock, in whom in the course of four years there developed mental disturbances, epileptiform seizures, dysarthria and torsion dystonia. While he was under observation in the hospital, his behavior showed pronounced features of a hysterical trend, with exhibition of "paradoxical kinesis"; e. g., when hearing an orchestra playing in the street, he promptly left the bed and reached the window without showing dystonia; at other times he was bedridden because of involuntary movements. He died of bronchopneumonia. Autopsy revealed an osteosarcoma infiltrating the sacral plexus. Histologic examination of the brain showed a diffuse inflammatory process (perivascular infiltration with the Hortega cells, glial proliferation and neuronophagia) in the cerebral cortex, especially in the frontal lobes, but no abnormalities of note in the basal ganglions or elsewhere. The liver was not affected. Munch-Petersen discusses the theories of pathogenesis of torsion dystonia and comments on the clinicopathologic observations in his case as follows: The diffuse encephalitic process in the cortex led to a release of the extrapyramidal motor system in the form of torsion dystonia, without direct involvement of the basal ganglions; the basal ganglions were involved by a lesion not demonstrable by available methods, or torsion dystonia developed as a psychogenic (hysterical) defense reaction to the malignant tumor of the sacral plexus. While accepting the view that torsion dystonia is a syndrome of organic origin, he believes that psychogenic (hysterical) factors may play an important rôle in the "fixation" of extrapyramidal motor disturbances in the form of torsion dystonia. He points out the prominence of the psychic component in the symptomatology of all extrapyramidal syndromes.

YAKOVLEV, Palmer, Mass. [ARCH. NEUROL. & PSYCHIAT.]

PROGNOSIS OF CONVULSIVE FITS IN CHILDHOOD. N. FAXÉN, Nord. med. tidskr. **11**: 81 (Jan. 18) 1936.

Faxén has tried to evaluate the degree of certainty with which epilepsy and other organic cerebral diseases can be diagnosed or ruled out in children with convulsions. In 95 children admitted to a hospital for observation epilepsy had been diagnosed, and of these 15 had been free from any symptoms during at least three years. Of 234 children with convulsions in connection with acute infections, regarded as nonepileptic, 12 were found to have epilepsy (6 had psychic debility). In 7 other children there was no epilepsy, but there was imbecility. Of 23 who were regarded as having psychogenic seizures, none was found to be epileptic or imbecile. Thus, of 257 children in whom the convulsions were thought to be of purely functional origin, 7 per cent were suffering from conditions which had been incorrectly diagnosed (12 children were epileptic; 7 were imbecile).

WALLGREN, Gothenburg, Sweden.

PROGRESSIVE HEREDITARY CEREBRAL LEUKODYSTROPHY. R. FORSBERG and R. STRØMNE, Norsk mag. f. lægevidensk. **97**:261 (March) 1936.

A detailed description is given of four children of the same family who early in life began to show neurologic symptoms: ataxia of the cerebellar type, spasticity of the arms and legs, pes cavus, disorders of speech and also psychic defects.

The disease was progressive. Another child in this family, a girl, now aged 21, showed rigidity of the legs and nystagmus. Only one child of the family was quite healthy. Two cousins are sick in the same way. The parents are healthy, but a sister of the grandmother seems to have the same disease, which Forsberg and Strømne call "leucodystrophia cerebri hereditaria progressiva."

WALLGREN, Gothenburg, Sweden.

EPILEPTIC CONVULSIONS AFTER POSTVACCINAL ENCEPHALITIS. ERIK LINDE, Svenska läk.-tidning. **33**:193 (Feb. 14) 1936.

A boy aged 14 months was treated at the pediatric clinic of Lund, Sweden, in 1928 for postvaccinal encephalitis and was discharged healthy. During the first two years thereafter he remained in good health; then he began to have fits of petit mal, from ten to fifteen attacks every year. In 1934 general convulsions with loss of consciousness occurred. The epilepsy was regarded as caused by cerebral changes produced by the encephalitic process.

WALLGREN, Gothenburg, Sweden.

HYDROCEPHALUS CAUSED BY OBSTRUCTION OF THE AQUEDUCT OF SYLVIUS. C. DE LANGE, Maandschr. v. kindergeneesk. **5**:159 (Jan.) 1936.

In a baby, meningomyelocele and hydrocephalus were found. The hydrocephalus constantly increased, and the meningomyelocele began to ulcerate. At the age of 13 months the child died. On microscopic investigation of the brain meningo-encephalitis was found with obstruction of the aqueductus Sylvii by a glia membrane. The meningo-encephalitis must have been an acute process issuing from the ulcerating meningomyelocele, whereas the obstructing membrane, Lange explains, was a consequence of a fetal process of inflammation.

VAN CREVELD, Amsterdam, Netherlands.

A NOTE ON THE SIGNIFICANCE OF INFANTILE NUTRITIONAL DISTURBANCES IN THE DEVELOPMENT OF ALCOHOLISM. B. S. ROBBINS, Psychoanalyt. Rev. **22**: 53 (Jan.) 1935.

Robbins calls attention to what he regards as a neglected factor in the development of alcoholism, namely, the relationship existing between general nutritional disturbances and addiction to alcohol. Digestive disturbances, loss of appetite and indisposition to take food, as well as violent ejections, are widely known accompaniments of the alcoholic spree. The discussion is based on a psychoanalytic study in the case of a man aged 26, in whom early nutritional disturbances played a significant rôle in the later development of alcoholism. As a spontaneous attempt at healing, alcoholism developed subsequent to a breakdown in adolescence, panic-like in character, with marked obsessional and compulsive features. The underlying neurosis appeared to be definitely linked to a prolonged period in infancy and childhood characterized by malnutrition and eccentricities in feeding. To avoid feelings of guilt, the patient threw himself into riotous living, with excessive consumption of alcohol as an expedient. He always insisted that alcohol was a life-saver for him. During a period of abstinence from liquor, fogginess, unreality and withdrawal symptoms became prominent, and this was combined with the realization that alcohol was becoming less successful in warding off the "shakes" (terror fantasies). His earliest recollections at the age of from 3 to 4 years concerned a particular distaste for milk, violent rejections of most foods and hatred of those who forcibly fed him. He frequently induced vomiting and could tolerate only foods of thick consistency. By virtue of the feeding difficulties, he was considered a delicate child and was much pampered and overprotected. Nevertheless, life was grim and bitter, and liquor was a means of inducing stupor and forgetfulness through its narcotic effect. Despite the fact that even as an adult he had no joy in eating, he was constantly preoccupied with food. He was never really hungry. Eating was with him a conscious, deliberate process. It

was as though something had occurred in the breast-mouth intimacy with his mother which had divorced the substantial aspects of feeding from the erotic, and living thenceforth became not a pleasure but a duty. He readily equated the alcoholic bottle with the breast, and there was reason to surmise that deprivations must have occurred singularly early. The craving was much like that of a starved child for milk. He could not, however, understand why, if he wanted it so insistently unconsciously, he found it so repulsive in reality.

In the course of treatment the patient realized that behind this great hostility for his mother there must have been a time when he thoroughly enjoyed her. He then recalled, not as an actual experience but as hearsay, that in the first few days after birth his mother had been profoundly ill and had had an abscess of the breast which necessitated the patient's weaning. After this withdrawal his life was despaired of for many months. He was subject to pylorospasm with violent regurgitations and could retain only a heavy, gruel-like substance. Of significance is his comment that this substance seemed much like the material which was exuding from his mother's breast during the first few days she had nursed him (colostrum). The subsequent attitude toward his mother and others is understood by the fact that he was left alone and starving at the time of his greatest need.

KARPMAN, Washington, D. C. [ARCH. NEUROL. & PSYCHIAT.]

Psychology and Psychiatry

ASSISTANCE FOR EPILEPTICS OF SCHOOL AGE. G. PAUL-BONCOUR, Rev. franç. de puériculture **3**:239, 1935.

Paul-Boncour emphasizes the need for proper educational facilities for epileptic children of normal or only moderately retarded mentality. These facilities are best provided in institutions exclusively for epileptic patients in which the children are separated into different groups according to their mental capacity and in which there are daily medical supervision and instruction adapted to the individual child.

CRANE, Chicago.

EDUCATIONAL AND STATISTICAL DATA ON CHILDREN OF ABNORMAL MENTALITY IN THE ELEMENTARY SCHOOLS OF FLORENCE. V. UGUCCIONI, Riv. di clin. pediat. **33**:1245 (Nov.) 1935.

In a brief historical outline Uguccioni reports that the first institution in Italy for the education of abnormal children was established in Aosta in 1848; it accommodated the cretins in this region, and the asylum was closed after a short existence. In 1884 an asylum for the education of imbecile and idiot children was established in Sicily but was later transformed into a custodial institution. The first real educational institution for feebleminded children was established in Liguria, in 1889. Then other institutions were built in Milan, Alexandria and Rome.

The facilities are discussed for the education of feebleminded children in the following Italian cities: Turin, Genoa, Milan, Bologna, Rome, Naples and Palermo, Sicily. From 1 to 4 per cent of the school children utilize these special facilities.

The school established in Florence is described in detail. There are seven hundred and twenty pupils in this school. Intensive medical study of the children in these classes is essential for efficient educational procedures.

HIGGINS, Boston.

SIGNIFICANCE OF THE AGE OF THE PARENTS AND ORDER OF BIRTH IN THE ETIOLOGY OF SUBNORMAL MENTALITY. EMILIE KLEINDIENST, Monatschr. f. Kinderh. **64**:24, 1935.

In a group of children from forty-eight families with no known hereditary stigmas, the fifth child of the family seemed below normal physically. This child was usually born when the mother was over 30. On the other hand, mental subnormality developed most frequently in the first-born in this series (in 50 per cent).

There is a temptation to ascribe the condition in the first-born infant to injury at birth. Whether or not the mother is past 30 must also be considered. Unquestionably, medical literature tends to the idea that the older the mother the more likely the first child is to be defective.

Elimination of hereditary factors and acceptance of the idea that the defective first child is the result of birth injury aid the physician in advising parents as to the desirability of subsequent children. A second defective child is exceedingly rare in a family with no history of nervous disease. Parents should be urged to have other children unless the mother is too old. (The reviewer gathers that the author considers the age of 30 to be the dividing line.) GERSTLEY, Chicago.

CONGENITAL WORD BLINDNESS FOLLOWING INJURY AT BIRTH. T. BRANDER, Monatschr. f. Kinderh. **64**:55, 1935.

The author describes a case of congenital word blindness in association with slight mental subnormality. He diagnosed the condition as due to injury at birth, as no similar cases had occurred in the family and as immediately after birth the child showed signs of asphyxia and later refused to nurse. The intracranial hemorrhage was probably due to the fact that the child was a twin and was born prematurely and delivered by forceps.

The author suggests that in all such cases careful physical examination should be made to determine whether or not the mental abnormality is the result of intracranial hemorrhage. GERSTLEY, Chicago.

REMARKABLE CASE OF ERETHISM IN CHILDHOOD. THEODORE HELLER, Ztschr. f. Kinderpsychiat. **2**:45 (June) 1935.

A case is reported in a 9 year old boy. He was born after a difficult labor and suffered from convulsions during the first few weeks of life. His infancy was stormy. Development was slow and speech scanty (syllabic). There was high grade erethism. The boy was always restless and in motion. Coarse movements were always accompanied by choreiform restlessness affecting all the muscles of the body. The child was stubborn and unmanageable and had terrific tantrums. Far from improving, he grew steadily worse. Medical opinion attributed the condition to trauma at birth.

On physical examination the boy was underdeveloped, pale and undernourished. The limbs were short and out of proportion to the large hands and feet. There were moderate hydrocephalus, evidence of rickets, a high arched palate and adenoids. A diagnosis of chondrodystrophy was made. In spite of all the forms of therapy used the erethism was not improved. The purposeless and constant activity without fatigue cannot be explained.

In spite of his physical and emotional handicaps the boy possessed remarkable manual dexterity and could untie a knot regardless of its complexity and fit keys into unknown locks with unbelievable swiftness. He was skilful with building-blocks. Of particular interest was his uncanny ability to locate hidden objects, regardless of size or place. In scholastic activities he made himself remarkable by seemingly paying little or no attention to the lessons, yet showing extraordinary aptitude in reading, writing and arithmetic. Though his vocabulary had improved, diction remained faulty. His restlessness continued in the schoolroom. He was accustomed to rise suddenly, run around the room, make a few purposeless, ticlike movements and return to resume his work.

This case is highly atypical, as erethism in association with mental deficiency is usually characterized by mental deterioration. In this case the mental faculties appeared definitely accelerated. JAHR, Omaha.

YOUTH IN THE CULTURAL CENTERS IN CITIES. M. FRIEDLANDER, Zycie Dziecka **4**:1 (Jan.) 1935.

Present culture is in reality the culture of big cities. The life of youth in the cultural centers in big cities reflects on smaller towns and provinces through radios, newspapers, automobiles, sports and politics. These cultural centers are great agencies for the development of youth physically, morally and spiritually. However, they are very often associated with selfish motives. Often they take advantage of youth for the promotion either of religious ideals or of public, financial or political ends. Such abuses of youth are found to a greater extent in countries like Russia, Italy and Germany. Poland, however, wants to profit by the mistakes of other countries and develop the cultural centers along unselfish lines.

Much has been accomplished in Poland, but much has to be done in the future.

KRUPINSKI, Chicago.

SCOUT LIFE AND ITS SIGNIFICANCE. S. HRYNIEWIECKI, Zycie Dziecka **4**:8 (Jan.) 1935.

Poland realizes the value of scout life (*Harcerstwo*) for its school children. The program of the nation is to have 80 per cent of the school children belong to the organization of scouts. In Poland this organization is controlled by the government, which encourages the public to support the movement to the limit, because the benefits that the child derives are enormous. Scouting molds character, stimulates ambition, teaches responsibility. In other words, the child profits physically, mentally and spiritually. Scouting is the school which develops active future citizens; therefore, it should be supported by all. KRUPINSKI, Chicago.

PROBLEMS OF YOUTH IN POLAND AFTER SCHOOL. E. HRYNIEWICZ, Zycie Dziecka **4**:71 (March) 1935.

The problem of taking care of youth in the out of school season in Poland is very great. The difficulty that confronts the government and the public lies in the fact that the country is poor. The government budget in relation to this type of problem decreases every year. Government and private organizations can take care of only a small number of young persons, whereas about three million young persons in cities and in farming districts are neglected in the out of school season. From these facts it is very evident that the government and private welfare organizations have a great task to perform in the future. KRUPINSKI, Chicago.

Diseases of the Genito-Urinary Tract

RENAL AND URETERAL ANOMALIES. W. W. FUREY, Illinois M. J. **70**:281 (Sept.) 1936.

Furey reviews the renal and ureteral anomalies which may be diagnosed by the use of intravenous and excretory urography and reports personal experiences.

BARBOUR, Peoria, Ill.

THE PLASMA LIPIDS IN CHRONIC HEMORRHAGIC NEPHRITIS. I. H. PAGE, E. KIRK and D. D. VAN SLYKE, J. Clin. Investigation **15**:101 (Jan.) 1936.

By the gasometric method of Kirk, Page and Van Slyke, single or repeated determinations of the different lipid fractions were made on the blood plasmas of thirteen patients with chronic hemorrhagic nephritis whose renal damage varied from slight, with nearly normal urea clearance, to almost complete destruction, with only 3 per cent of the normal clearance. In the chronic active stage of the disease there was a tendency toward lipemia, while in the terminal stage the lipemia decreased, and before death it sometimes fell below normal. The individual lipid

constituents, free cholesterol, cholesterol esters, phosphatids and the neutral fat fraction, rose and fell together. There was no parallelism between lipemia and deficit in plasma protein, although both accompany the nephrotic syndrome.

GUEST, Cincinnati.

OBSERVATIONS ON THE NATURE OF THE SERUM PROTEINS IN NEPHROSIS. E. GOETTSCH and E. B. REEVES, J. Clin. Investigation **15**:173 (March) 1936.

Data obtained by the quantitative precipitin method indicate that during the edematous stage of nephrosis the serum proteins differ immunologically from normal serum proteins, in that both albumin and globulin fail to precipitate completely with antiserums developed against normal serum albumin and normal serum globulin. Globulin isolated from nephrotic serum is capable of stimulating an antibody response in rabbits, and the antiserum formed is not identical with that formed against globulin obtained from normal serum.

FROM THE AUTHORS' SUMMARY.

GENESIS OF RENAL CALCULI (PATHOLOGICAL-PHYSIOLOGICAL CONSIDERATIONS). A. RANDALL, New York State J. Med. **36**:1 (Jan. 1) 1936.

The various theories are interestingly reviewed. The dietary theory of the formation of stones is supported by the fact that the liberalization of children's diets has caused stone of the bladder to become a rarity in children. In England in 1800, 45 per cent of calculi occurred in children under 14 years of age. In countries where diets are still limited, calculi are still common in children. Diets deficient in vitamin A tend to produce stones. Infection plays a very definite part in the formation of some stones. Stasis and faulty drainage must also be considered, especially in bedridden patients—for example, children with tuberculous lesions of the spine. Claims are also put forward for the theory that a disturbance in the colloidal mechanism of the urine is a factor. Disease of the parathyroid glands is also blamed.

AIKMAN, Rochester, N. Y.

TREATMENT OF UNDESCENDED TESTES BY THE ANTERIOR PITUITARY-LIKE PRINCIPLE FROM THE URINE OF PREGNANCY. A. GOLDMAN, A. STERN and J. LAPIN, New York State J. Med. **36**:15 (Jan. 1) 1936.

Eleven boys were treated by injection of the anterior pituitary-like gonadotropic principle of the urine of pregnant women. Good results were obtained in ten cases; the one failure was in a patient of 23 years with a completely abdominal left testicle.

AIKMAN, Rochester, N. Y.

TREATMENT OF B. COLI PYELITIS WITH ALKALIS. A. A. OSMAN, Brit. M. J. **1**: 575 (March 21) 1936.

Osman outlines his method of treating pyelitis due to B. coli with alkalis and gives a general discussion of the matter. He thinks there is little danger that alkalosis will supervene. He stresses the point, however, that little or no benefit can result from this treatment if there is any obstruction in the urinary tract.

ROYSTER, University, Va.

PREGNANCY IN A GIRL WHO HAD NEVER MENSTRUATED. BUÉ. R. PALLIEZ and L. GERNEZ, Bull. Soc. d'obst. et de gynéc. **25**:147 (Feb.) 1936.

A girl 12 years old was taken to a physician for examination because the parents had observed progressive enlargement of her abdomen. Pregnancy was diagnosed, although the menses had not yet been established. A 32 year old boarder was suspected of relations with the child. She was 136 cm. tall and weighed 39 Kg. The physical examination of the child, especially from the

obstetric angle, is discussed in detail, and a photograph shown. The infant was delivered, at term, by cesarean section because of the mother's contracted pelvis. The infant weighed 2,900 Gm. The authors state that pregnancy in a girl of this age is rare in their country. Of 17,500 deliveries over a period of sixteen years in one hospital in Lille only 9 mothers were 15 years of age or less. The literature is briefly reviewed.

GLASER, Rochester, N. Y.

LIPOID NEPHROSIS IN A SEVEN MONTH OLD INFANT. S. MENDIVIL, Arch. de pediat. d. Uruguay **2**:208 (May) 1936.

A 7 month old infant without previous history of significant illness, exclusively breast fed, presented massive edema and severe albuminuria, which reached 14 Gm. per thousand cubic centimeters. Also the urine contained doubly refractory crystals. The blood cholesterol was normal, and the plasma proteins could not be investigated. There were no evidences of infection. Later, casts and red blood cells were found in the urine. A month after the onset the child experienced intercurrent nasal diphtheria, which responded satisfactorily to serum therapy. After marked improvement of the general condition the infant contracted an infection of the upper respiratory tract, which precipitated a fatal termination. The nephrosis was treated by thyroid extract. This was the youngest patient with lipoid nephrosis that had ever been reported to the Pediatric Society of Montevideo.

SCHLUTZ, Chicago.

HEREDITY IN HYPOSPADIAS. F. STEINER, München. med. Wchnschr. **83**:1271 (July 31) 1936.

Hypospadias is a congenital malformation. It occurs once in every three hundred male infants, according to Kaufmann, and once in every thousand male infants, according to Neugebauer. A familial occurrence has been observed numerous times, and the direct transmission of this condition through several generations has been reported. Rumpel in 1921 reported hypospadias in monozygotic twins. Steiner now reports the second such observation in identical twins. There was no history of hypospadias in the family. Although it is possible that the occurrence of hypospadias in both twins may have been a coincidence, still the observation of several cases in certain families and the previous observation in identical twins make it likely that heredity is an important factor.

BRAHDY, Mount Vernon, N. Y.

CYST OF THE KIDNEY AND CARCINOMA OF THE KIDNEY. M. SIMONSEN, Röntgenpraxis **8**:32 (Jan.) 1936.

The first case was that of a renal cyst in a 4 year old child. Roentgenographic examination with a contrast medium (skiodan) led to the diagnosis of a tumor of the lower pole of the left kidney. Operation disclosed a double kidney; the lower member was hydronephrotic and had produced some obstruction of the outflow of urine from the upper kidney. The second case was one of a cystic carcinoma of the kidney in a 61 year old man.

MCCUNE, New York.

ECTOPY OF THE KIDNEY. T. CANIGIANI, Röntgenpraxis **8**:103 (Feb.) 1936.

By the use of a contrast medium, the right kidney of a patient was found to lie just beneath the left kidney; the ureter crossed the midline and emptied into the right side of the bladder. The ectopic kidney was somewhat hydronephrotic. In cases of this sort the displaced kidney is occasionally found fused to the normally placed one.

MCCUNE, New York.

HEMATOPORPHYRINURIA. SVEN SALÉN, Nord. med. tidskr. **11**:151 (Jan. 25) 1936.

A boy aged 10, who was of a healthy family, fell ill after tonsillitis, with recurring pains in the abdomen, followed a week later by hematuria, meningism (cerebrospinal fluid normal), fever and flaccid paralysis of the arms and legs. He was seen seven months after the onset of the disease. He then had atrophy of the muscles of the extremities, tachycardia and paroxysmal pains in the abdomen. The urine was clear but red-brown and contained porphyrins and a few red and white blood cells. The color of the urine varied, some days being normal and other days light red-yellow to dark red-brown. When it was normal, the reaction was neutral or alkaline; when it was dark, the reaction was acid. No abnormal pigmentation of the skin was present. The condition of the boy was considerably improved during the month he was treated at the hospital.

WALLGREN, Gothenburg, Sweden.

SPINA BIFIDA OCCULTA AND ENURESIS NOCTURNA. O. ANDERSON, Ugesk. f. læger **98**:534 (June 11) 1936.

In a group of twenty-five children with enuresis nocturna, 80 per cent showed roentgenologic defects in the lumbosacral segment of the spinal column. An equal group of normal children gave the same findings in 64 per cent. This result agrees with those of other investigators, and Andersen draws the conclusion that abnormalities of the vertebral column without neurologic findings have no causal significance in enuresis nocturna.

ELGHAMMER, Chicago.

Diseases of the Ductless Glands; Endocrinology

THE CALORIGENIC ACTION OF EXTRACTS OF THE ANTERIOR LOBE OF THE PITUITARY IN MAN. W. O. THOMPSON and others, Endocrinology **20**:55 (Jan.) 1936.

The following facts regarding the relationship between the pituitary and the thyroid gland have been demonstrated in animals:

1. Enlargement of the pituitary gland has been noted in thyroidectomized animals.

2. The thyroid gland becomes atrophic, and the basal metabolism drops, following removal of the pituitary gland.

3. Active extracts of the pituitary gland cause (*a*) hyperplasia of the thyroid gland, (*b*) reduction of the iodine in this gland, (*c*) increase in the organic iodine in the blood, (*d*) tachycardia, (*e*) exophthalmos and (*f*) increase in the basal metabolic rate. These changes do not occur in thyroidectomized animals.

4. Iodine is effective in reducing the high basal metabolism of animals which are receiving pituitary extracts.

5. The metabolic and thyroid changes produced by pituitary extracts are always temporary, and prolonged administration in animals may cause the metabolism to drop to as low a level as that seen after hypophysectomy. The serum of such animals contains some factor which inhibits the action of the thyrotropic principle. This observation has given rise to the antihormone theory of Collip.

Only in isolated instances have such observations been made in man. Therefore the effect of the administration of various pituitary preparations to fifty-nine patients was studied.

When extracts containing the thyrotropic principle were given, an increase in basal metabolism was noted in every patient in whom there was any thyroid tissue capable of functioning. Patients with nontoxic goiters could be made toxic, but no rise in toxicity was noted in four patients with myxedema.

The increase in metabolism was always temporary. Second courses of treatment usually failed to produce any increase.

Thyroxin U. S. P. and thyroid U. S. P. produced well marked calorigenic effects after the patients had become refractory to the pituitary extracts.

JACOBSEN, Buffalo.

ENDOCRINE DWARFISM. R. L. SCHAEFER, Endocrinology **20**:64 (Jan.) 1936.

In this paper the four dwarfs discussed in two previous papers are reported on after two years and nine months of observation, and seven others treated for from six to nineteen months are also described. Growth in height in excess of the normal for the individual age and period of treatment has been induced.

Complete studies of the metabolism in these eleven cases of pituitary dwarfism are recorded. The body measurements are below the minimal normal but are proportionate. Generalized chondro-epiphysial changes, including such conditions as Schlatter's, Perthes' and Köhler's disease, are not an infrequent finding.

JACOBSEN, Buffalo.

PITUITARY CACHEXIA (SIMMONDS' DISEASE). R. C. MOEHLIG, Endocrinology **20**:155 (March) 1936.

A 15 year old school girl was seen with the following complaints: loss of weight and strength, decaying teeth, falling hair, irregular menstruation, metrorrhagia, mental lethargy, dryness of the skin and marked anorexia. These symptoms were of ten months' duration.

The father weighed 245 pounds (111 Kg.), the paternal grandmother 235 pounds (107 Kg.), and the mother 200 pounds (91 Kg.). The child's weight had been 162 pounds (119 Kg.) and was 134½ pounds (106 Kg.) at the time of her first visit.

One year after onset her weight was 101 pounds (91 Kg.), and muscular atrophy was everywhere extreme. The heart was small; the blood pressure, low. Muscular weakness was marked. The temperature was repeatedly 94 F.

She was treated with the gonadotropic hormone from the urine of pregnant women (antuitrin S), an extract of adrenal cortex (eschatin), insulin alone and with dextrose, pituitary tablets, cod liver oil, sunshine, a diet high in calories and forced feeding. Despite these various forms of endocrine gland therapy and supportive measures, she died seventeen months after the initial symptoms began.

JACOBSEN, Buffalo.

THE DIFFERENCE OF RESPONSE OF MALES WITH UNDESCENDED TESTES TO THE WATER SOLUBLE (ANTERIOR PITUITARY-LIKE) FRACTION OF PREGNANCY URINE. H. S. RUBINSTEIN, Endocrinology **20**:192 (March) 1936.

Eight boys from 9½ to 17 years old were treated with gonadotropic hormone from the urine of pregnant women. Three possessed normal anthropomorphic proportions. The changes observed in the other five fell into the class of constitutional dysplasias, with the infantile type of genitalia, Fröhlich's syndrome, etc.

The three boys who showed no obvious endocrinopathy in addition to the delay in the descent of the testes did not respond favorably to treatment. In one of these, exploratory operation failed to reveal testes; in another, a hernia was present. In all five boys with involvement of the pituitary gland a good response was obtained.

It is suggested that the water-soluble fraction of the urine of pregnant women seems to induce descent of the testes in man only if the pituitary gland is sexually underactive. The administration of this substance then leads predominantly to a stimulation of the interstitial cells of the testes and results in descent if mechanical obstruction does not exist.

JACOBSEN, Buffalo.

OBSERVATIONS ON ADRENAL INSUFFICIENCY. J. STAHL, D. W. ATCHLEY and R. F. LOEB, J. Clin. Investigation **15**:41 (Jan.) 1936.

From studies of the metabolism and chemical studies of the blood of a doubly adrenalectomized dog during a period of two years the following conclusions were drawn: 1. The decrease in the concentration of sodium and the increase in that of urea in the blood in adrenal insufficiency are not interdependent, although

they are frequently encountered simultaneously. 2. A withdrawal of salt from the diet of the adrenalectomized dog when the animal was being maintained with cortical extract resulted in an increase in the blood urea and a decrease in the blood sodium, as did a withdrawal of cortical extract. 3. A marked reduction in the ingestion of salt failed to influence the concentration of sodium and of urea in the blood when an unusually potent preparation of cortical extract was employed. 4. A withdrawal of salt from the diet or a withdrawal of cortical extract caused a decrease in renal function. 5. The administration of a single large dose of cortical extract in severe adrenal insufficiency caused striking improvement in the general well-being of the dog before any consistent changes could be determined in the concentration of sodium, potassium or urea in the blood or in the water content of the serum.

GUEST, Cincinnati.

DIABETES INSIPIDUS. J. H. BIGGART, Brain **58**:86, 1935.

Since Thomas Willis (1674) differentiated between diabetes mellitus and diabetes insipidus, there have been three main epochs in the history of the syndrome of diabetes insipidus. The first dates from 1860, when Claude Bernard produced a similar syndrome in rabbits by puncture of the floor of the fourth ventricle. Other investigators verified this observation, and more recently Dresel and Lewy (1924) concluded that the area concerned was in the floor of the fourth ventricle, medial to the spinal tract of the trigeminal nerve, ventromedial to the restiform body and dorsal to the nucleus of the seventh nerve. The second period in the history of the disease may be said to have followed the work of Schäfer and Magnus (1901 and 1906) and Herring (1908) on the active principle of the posterior lobe of the hypophysis and its relation to diuresis. Cushing (1910 and 1914) produced the syndrome by hypophysectomy, while Farini and van der Velden (1913) showed the controlling influences of injections of solution of posterior pituitary on polyuria. It became widely accepted that the syndrome was the result of hypofunction of the posterior lobe of the hypophysis. The third and present theory of the pathogenesis of the syndrome was initiated by Camus and Roussy (1913) after the work of Aschner (1917), who showed that hypophysectomy in itself does not produce polyuria but that in animals in which the syndrome developed microscopic examination always reveals a lesion in the floor of the third ventricle. This view has been verified by others, who succeeded in producing polyuria by injuring the infundibulotuberal region.

In an attempt to correlate these observations, Biggart analyzed three cases presenting the syndrome of diabetes insipidus. The pathogenesis in the cases varied from trauma following operation for adenoma of the pituitary gland to metastatic malignant disease and encephalitis. All the cases had in common a lesion of the hypothalamus, while in the first two instances there was a concomitant lesion of the hypophysis. Polyuria in the first two cases was controlled by injections of solution of posterior pituitary, while in the third the condition did not respond to this treatment.

In the light of recent anatomic observations, Biggart noted on histologic study that in two cases the supra-opticohypophysial tract was interrupted by the lesions, the cells of the nucleus tuberalis and nucleus supra-opticus being largely intact. In both instances the pars tuberalis was involved. In the third case there was destruction of both the nucleus tuberalis and the nucleus supra-opticus, with inflammatory involvement of the pars tuberalis. Since the polyuria was controlled by injections of solution of posterior pituitary in two cases and not in the third, there seems to be proof for assuring a central action for the antidiuretic factor. That it is the tuberal nuclei through which the action takes place is rendered probable by the existence of the tractus tuberalis descendens and by consideration of the experimental work of the French school.

SALL, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

CRETINISM, WITH UPPER LUMBAR KYPHOSIS RESEMBLING THAT IN MORQUIO'S DISEASE. W. SHELDON, Proc. Roy. Soc. Med. **29**:500 (March) 1936.

The case reported was that of a child of 23 months, the fifth of six children of healthy parents. The previous history, the history at the time of admission to the hospital, the condition on admission, a photograph of the child and the x-ray plate are included in the report.

Roentgen examination showed kyphosis and a tonguelike projection of the lower part of the second lumbar vertebra and to a less extent of the first lumbar vertebra. Kyphosis in the upper lumbar division of the spinal cord seems to be constant in the osteochondrodystrophy of Morquio.

WILLIAMSON, New Orleans.

HYPOPHYSIAL ORIGIN AND GENESIS OF MARFAN'S SYNDROME. J. FRANÇOIS, Ann. d'ocul. **172**:700 (Aug.) 1935.

In a patient with Marfan's syndrome who had ectopia of the crystalline lens, François noted various symptoms of involvement of endocrine glands which permit association of this disease with hypophysial dystrophy. The fundamental symptom was gigantism, which must be caused by hypersecretion of the hormone of growth by the eosinophilic cells. In addition to hyperfunction, there were other symptoms of insufficiency of secretion of the basophilic cells, the number or activity of which was diminished. These symptoms were: aplasia of the genital organs and absence of hair, decrease in the basal metabolic rate, reduction of the urea and urinary excretion, a generally slender exterior aspect, absence of cellulofatty tissue, lack of muscular development, hypotension, hypocholesteremia, hypoglycemia and increase in sugar tolerance.

François believes that in all cases Marfan's syndrome must be associated with hypophysial dystrophy. This disease is related to acromegaly and hypophysial gigantism. The differentiation of these three disorders depends solely on the age at which the disease appears; e. g., Marfan's syndrome appears in the embryo, gigantism in the adolescent and acromegaly in the adult.

BERENS, New York. [ARCH. NEUROL. & PSYCHIAT.]

THE ROENTGEN SHADOW OF THE ENLARGED THYMUS. M. LAMY, Bull. Soc. de pédiat. de Paris **34**:145 (March) 1936.

A few ordinary anteroposterior views of infants with enlarged thymuses are reproduced. The widening of the shadow during expiration is demonstrated. Not infrequently autopsy reveals that the interpretation of mediastinal widening as due to enlargement of the thymus is incorrect.

BENJAMIN, Montreal, Canada.

THYROPARATHYROIDECTOMY AND DIFFUSIBLE SERUM CALCIUM. C. ROERSCH, Compt. rend. Soc. de biol. **118**:809, 1935.

The opinions of various authors are quoted relative to the effect of parathyroidectomy on the fixed and ionic calcium in the serum. No modification occurs, according to von Meysenbug and McCann; diminution of both occurs, according to Salveson and Linder, Moritz, and Pincus, Peterson and Kramer.

Roersch performed parathyroidectomy on five dogs and noted rapid development of tetany and hypocalcemia, the calcium descending to 6.01 mg. in two days; at the same time there was produced about a 20 per cent increase in the nonfixed or diffusible calcium in the blood.

WAHL, Cleveland.

LOCAL LIPOMATOSIS AFTER INJECTIONS OF INSULIN. R. PRIESEL, Arch. f. Kinderh. **106**:1, 1935.

The results of gross and microscopic examination of lipomas formed at the site of injections of insulin in a diabetic child are described.

CRANE, Chicago.

Diseases of the Muscles, Bones, Joints and Lymph Glands

METABOLIC STUDIES IN OSTEOPOROSIS. M. ADAMS, W. M. BOOTHBY and A. M. SNELL, Am. J. Physiol. **114**:383 (Jan.) 1936.

This is a report of an extensive study of the metabolism of a subject with osteoporosis of a senescent type, the chief object of which was to compare the utilization of the calcium in calcium lactate and in tribasic calcium phosphate. The results indicated that the soluble calcium lactate could be assimilated more readily than the insoluble calcium phosphate. A definite clinical improvement accompanied the storage of calcium and phosphorus.

NOURSE, Cleveland.

HODGKIN'S DISEASE OF THE SCALP: REPORT OF A CASE. N. M. WRONG, Arch. Dermat. & Syph. **33**:259 (Feb.) 1936.

Wrong reports the case of a boy of 12 years who had a flat tumor of the scalp, which measured 10.5 by 7.5 by 1 cm. The only other positive findings were five small hard lymph glands in the left posterior triangle of the neck. Biopsy of the tumor of the scalp led to a diagnosis of Hodgkin's disease by three eminent pathologists, though a lesion of Hodgkin's disease at this site is extremely rare. The tumor of the scalp and the palpable lymph glands of the neck responded to three very small doses of roentgen rays, an observation which was further in favor of the diagnosis.

DULIN, Iowa City.

X-RAYS IN CHRONIC RHEUMATIC ARTHRITIS: DIAGNOSIS, PROGNOSIS AND TREATMENT. S. GILBERT SCOTT, Brit. J. Phys. Med. **10**:127 (Dec.) 1935.

The value of roentgenology in the differential diagnosis of the various types of arthritis and in differentiating other conditions from arthritis is stressed. The remarks on treatment are centered chiefly on local treatment of chronic osteoarthritis. A technic for treatment with roentgen rays is described. It is said that the method is known to have resulted in the disappearance of loose bodies from the joint.

HARTMAN, Cleveland.

HISTAMINE INJECTIONS IN CHRONIC RHEUMATISM. B. SHANSON, Brit. J. Phys. Med. **10**:185 (March) 1936.

Shanson summarizes the bibliography on the use of histamine in the treatment of chronic rheumatism. He uses from 0.1 to 0.5 cc. of a solution of histamine acid phosphate made up in the strength of 1 mg. to 1 cc. of physiologic solution of sodium chloride. He gave daily subcutaneous injections, increasing the dose until a reaction, characterized chiefly by flushing, occurred. The dosage was continued, with daily or biweekly injections according to the response. He thinks that the use of histamine appears to be indicated when there is restriction of movement other than that due to pain, when there are vasomotor symptoms or when a superimposed functional element is suspected. It is said that the results are sometimes dramatic and lasting but that often they are transient and disappointing.

HARTMAN, Cleveland.

TWO CASES OF STILL'S DISEASE CURED BY GOLD INJECTIONS. W. S. C. COPEMAN, Proc. Roy. Soc. Med. **29**:497 (March) 1936.

1. A girl aged 8¼ years had suffered from pain and swelling of the knees with pyrexia in February 1934 and again in May, which had been controlled by means of salicylates. The condition progressed, and in December of the same year she was admitted to the hospital and given weekly injections of sodium aurothiopropanol sulfonate (0.05 Gm., at the beginning; 0.5 Gm., in all). After a fortnight she was reported to be moving her legs more easily. Five months later she was much improved, walking a little each day in outdoor shoes. Six months later the improvement was found to be fully maintained.

2. A boy of 14 years had suffered from rheumatic arthritis from infancy. He was given two courses of injections of gold salts. The condition seemed to clear up soon after the injections.

WILLIAMSON, New Orleans.

POSTTRAUMATIC OSTEOPATHY SIMULATING A SARCOMA. FÈVRE, GOUYEN and HUGUENIN, Bull. Soc. de pédiat. de Paris **34**:196 (March) 1936.

A boy 14 years old complained of pain in the region of the left great trochanter, which he said dated from a slight trauma a year previously. Roentgenograms of the femur showed cortical thickening and osteoporosis, with disappearance of the cortex at the inferior part of the great trochanter. A tentative diagnosis of sarcoma was entertained. A specimen was taken for biopsy, but no tumor cells were found in the sections examined. The condition was posttraumatic osteopathy resembling the localized Paget's disease which has been described in adults.

BENJAMIN, Montreal, Canada.

HYPERTROPHY OF THE LYMPHATIC GLANDS IN INFANCY. G. J. GINANDES, Paidoterapia **14**:813 (Jan.); 913 (Feb.) 1936.

Dr. Ginandes of the Mount Sinai Hospital, New York, describes the lymphoid tissue and its histologic structure. There is yet no general agreement as to all of the functions of the lymphoid tissue. Its function in lymphopoiesis and as a scavenging system is generally accepted. Its extreme importance in immunization has only recently been appreciated, and in this connection the secondary nodule has assumed an important rôle. The importance of the lymphatic system in transportation, more especially in relation to the intestinal tract, has given rise to the conception that the lymphatic system plays an important rôle in digestion. This rôle is thought to be not merely accidental; it suggests that the same process may in large part be responsible for the protective principle ascribed to the lymphatic system anywhere in the body. The frequency of enlargement of the lymph glands in infancy and childhood is not accidental. It depends on certain special physiologic and anatomic peculiarities belonging to this period of life, namely: the relatively low state of immunity of the child, the extensive distribution of lymphoid tissue, the readiness with which this tissue reacts to even mild infection, the importance of hereditary and familial traits, the influence of certain diatheses, the striking susceptibility to the exanthematous diseases and the importance of certain nutritional and allergic disturbances in childhood.

It is important to remember that practically all normal children have some palpable lymph nodes, and that not every enlarged lymph node signifies disease. It is reasonable to believe that some enlarged nodes attain their size as a physiologic response to the demand for protection of the organism. The limitations on the examination for enlargement of lymph glands must be borne in mind, especially where glands are hidden in the deeper tissues—for example, in the mediastinum, in the abdomen or in the deeper tissues of the extremities. Regional glandular enlargement as a reaction to infection in the area helps establish the locus of the disease. However, infection in one part of the body may produce enlargement of glands in another area.

For clinical purposes, the lymphadenopathies in childhood may be divided into four main groups: infectious, benign, malignant and metastatic lymphadenopathies:

1. Infectious lymphadenopathies: Acute; chronic; tuberculous; syphilitic; Hodgkin's disease; infectious mononucleosis.

2. Malignant lymphadenopathies: Lymphatic; myeloid; monocytic; eosinophilic, and mixed cell; leukemic; aleukemic; chloroma, and leukosarcoma; lymphosarcoma; reticulum cell sarcoma; large round cell (lymphoblastoma); small round cell (lymphocytoma); plasmacytoma.

3. Benign lymphadenopathies: Allergic; associated with hyperthyroidism and with status thymicolymphaticus.

4. Metastatic lymphadenopathies: Malignant metastases from foci of malignant growth elsewhere in the body, such as neuroblastoma, carcinoma, teratoma and Wilms' tumor.

In approaching a differential diagnosis one should analyze the following: (1) the character and nature of the lymphadenopathy; (2) the accompanying fever; (3) the blood picture; (4) the size of the spleen; (5) the results of biopsy, and (6) the results of roentgen examination and the response to roentgen therapy. Ginandes discusses the more common diseases of the lymph glands, their differential diagnosis and their treatment and mentions the conditions simulating enlargement of the lymph glands.

HERRON, Spokane, Wash.

DISK-SHAPED MENISCUS LATERALIS GENU AS A CAUSE OF SLIPPING KNEE. W. JAROSCHY, Beitr. z. klin. Chir. **161**:139, 1935.

Three cases of loose knee are described. In each was found an abnormal-appearing and relaxed lateral meniscus, the removal of which did away with jerkiness. Twice the meniscus formed a solid thick plate, and once, an abnormally broad and thick structure which was C-shaped and which showed a rupture.

In most of the operative cases discussed in the literature the cause was a disk-shaped lateral meniscus. This is the most common and typical cause of spontaneous *schnellenden Knee.*

Jaroschy also discussed the formation and presence of the lateral meniscus in the new-born and in the premature infant. He came to the conclusion there is no difference in form between this abnormality and that found in adults.

RUBIN, Boston.

SO-CALLED COXA VARA CONGENITA. B. SIMON, Beitr. z. klin. Chir. **161**:205, 1935.

Simon states that the alleged fetal and postfetal origin of so-called coxa vara congenita in intra-uterine bone disease is not accepted. The deformity begins after birth, especially during the first decade of life on account of rebuilding processes in the neck of femur.

Good results are obtained with subtrochanteric osteotomy, which results in quick recovery of the patient and elimination of the deformity.

RUBIN, Boston.

KYPHOSIS JUVENILIS (SCHEUERMANN'S DISEASE). H. SCHEUERMANN, Fortschr. a. d. Geb. d. Röntgenstrahlen **53**:1 (Jan.) 1936.

In this paper Scheuermann deals with that variety of kyphosis which occurs in adolescent persons and which has been termed "occupational kyphosis" or "muscular kyphosis." In 1920 he suggested that the process is analogous to that which results in Legg-Calvé-Perthes disease and offered the title "osteochondritis deformans juvenilis dorsi"; from a clinical point of view the term "kyphosis juvenilis" is better. The disease is a developmental one, which commonly affects two or three vertebrae and in which anomalous maturation of the limbus vertebralis plays the principal rôle. Impaction of the cartilaginous portion of the vertebra into the spongiosa, combined with defective growth of the vertebral body, leads to the formation of wedge-shaped vertebrae. In the early stages it is not possible to prophesy the outcome. The paper is well documented.

MCCUNE, New York.

THE ROENTGENOGRAPHIC DIAGNOSIS OF EWING'S SARCOMA. R. B. ENGELSTAD, Fortschr. a. d. Geb. d. Röntgenstrahlen **53**:462 (March) 1936.

Although the roentgenographic and clinical features of Ewing's sarcoma are usually fairly characteristic, both may be so atypical as to render diagnosis well nigh impossible without biopsy. Two illustrative cases are reported: The first was that of an 11 year old girl whose first symptoms were pain and swelling in

one heel. The roentgen findings suggested a solitary cyst of the os calcis. The correct diagnosis was brought to light when an attempt was made to treat the lesion surgically. In the second case the presenting symptoms were sciatic pain and paresthesia involving the left leg; all evidence pointed to inflammatory disease of the vertebral column. Operation disclosed the uncommon phenomenon of Ewing's tumor primary in the vertebral column. Although both patients manifested the characteristic temporary improvement after roentgen treatment, the final outcome was fatal.

McCune, New York.

Some Clinical Aspects of Osteochondritis Dissecans of the Hip Joint. E. Friedl, Röntgenpraxis **8**:16 (Jan.) 1936.

Of twenty-one cases of osteochondritis dissecans which Friedl observed in a single year, one occurred in a 14 year old child; the disease does not affect children under 12 years of age. Osteochondritis dissecans is one of the two possible outcomes of aseptic necrosis of an epiphysis; the alternative sequel is Perthes' disease (osteochondritis deformans juvenilis). In Friedl's material the disease was bilateral in more than half of the cases, occurred six times more frequently in males than in females and affected the hip almost as often as the knee. The disease may run its course without giving rise to symptoms; on the other hand, a sequestrum may form (joint mouse), which may be resorbed or may heal in situ. If healing is long delayed, the process may lead to arthritis deformans.

McCune, New York.

A Roentgenographic Method for Simultaneous Visualization of the Soft Parts and Bony Structures of the Skull in Profile. H. Franke, Röntgenpraxis **8**:43 (Jan.) 1936.

A technic is described by the use of which it is possible to obtain excellent roentgenographic portraits in which the relation of the soft tissues to the underlying bones is admirably visualized. The procedure is valuable in orthodontia.

McCune, New York.

Calcium and Phosphorus Metabolism in Osteomalacia. H. I. Chu and others, Chinese M. J. **50**:1 (Jan.) 1936.

A boy of 19 years has been followed in the orthopedic clinic since the age of 5, when his legs began to be deformed. There was slow progression, with increasing difficulty in walking in the following years, especially by the time he was 17. Roentgen examination showed that the whole skeleton was more or less osteoporotic, with irregular deposits of calcium and cystlike changes in the cortex of bones.

The calcium and phosphorus in the serum was within normal limits. The calcium metabolism was difficult to explain in the light of the extensive osseous changes. The urinary and fecal excretions of calcium and phosphorus showed a normal balance.

Parathyroid extract was given for a period in order to see the effect on the bone changes, but hypercalcemia was produced, with vomiting, collapse and death, even with moderate doses of the glandular extract.

Neff, Kansas City, Mo.

Hyperplasia Fascialis Ossificans Progressiva (Goto). T. Okamoto, T. Kano and S. Sugiyama, Orient. J. Dis. Infants **18**:91 (July) 1935.

The condition of a girl 22 months of age with a diagnosis of hyperplasia fascialis ossificans progressiva was followed by means of repeated biopsies of ossifying tissue. The tissue showed abnormal development and increase of musculofascial connective tissue with calcification. The phosphatase content of the ossifying

tissue bore a direct relation to the process of ossification. The blood calcium and phosphorus were increased, but there was a decrease in the retention of nitrogen, and no change in the excretion of creatinine.

KATO, Chicago.

Diseases of the Eye

MALFORMATIONS OF THE HUMAN EYE. P. KIEWE, Arch. f. Ophth. **135**:220 (March) 1936.

Two rare congenital anomalies are described: 1. In a girl 3 months old with the clinical diagnosis of glioma a thick strand of tissue connected the optic disk with a connective tissue membrane lining the posterior surface of the lens. The posterior fourth of this strand contained the fibers of the optic nerve, which projected far beyond the level of the retina. The retina around the base of the strand had attached itself to the latter for a short distance. The strand contained an independent complete circulatory system. Kiewe interprets this picture as that of persistence of the intercalary piece of the optic stalk (*Schaltstück*) of von Szily.

2. In a girl 3 years of age whose condition was diagnosed clinically as metastatic ophthalmia following diphtheria pathologic examination revealed, in addition to the metastatic ophthalmia, persistence of the canal of Cloquet and of the membrana capsulolenticularis. Moreover, the preequatorial portion of the retina had formed a ring-shaped fold which protruded toward the axis of the eyeball. The top of this fold almost touched the posterior surface of the lens, which had the abnormal shape known as lentiglobus posterior.

KRONFELD, Peiping, China. [ARCH. OPHTH.]

THE IMPORTANCE OF THE PHLYCTENULAS: REPORT OF CASES. R. G. POSTHUMUS, Klin. Monatsbl. f. Augenh. **96**:362 (March) 1936.

Posthumus reviews the present state of the etiology of phlyctenulas, their relation to tuberculosis, rosacea and other diseases, and their affiliation with allergic conditions. He reports eight cases of phlyctenula associated with rosacea, in some of which it was also associated with choroiditis or with iridocyclitis. He points out the apparent connection of several phlyctenular types of conjunctivitis and keratitis with disturbances of endocrine secretion and associated manifestations of the autonomous nerve system. The résumé of his eight cases of phlyctenula associated with rosacea prompts him to suspect a tuberculous basis. He differentiates between genuine allergic conjunctivitides, on one side, and scrofulosis and rosacea, on the other. He thinks the two latter forms may represent allergy against the antigen of tuberculosis.

STOLL, Cincinnati. [ARCH. OPHTH.]

Skin Diseases; Allergy

THE INCIDENCE OF FAVUS IN KENTUCKY. C. C. BARRETT, Arch. Dermat. & Syph. **33**:126 (Jan.) 1936.

That favus is uncommon among native-born Americans is generally accepted. Barrett reports seven families in which favus occurred. Twelve persons were affected, all of them native-born Americans living in eastern Kentucky. Barrett believes that the disease was "probably brought to this section by early settlers who came from a country where favus is fairly common; it has not spread to other parts of the country, and has never been previously recognized because of the isolated character of the Appalachian region."

DULIN, Iowa City.

CICATRIZING MORPHEA WITH ANKYLOSING ARTHRITIS AND OSTEOBLASTIC CHANGE: REPORT OF A CASE. S. CRAWFORD, Arch. Dermat. & Syph. **33**:506 (March) 1936.

The case of a girl 5 years old with acute progressive morphea (diffuse scleroderma) is reported. The skin was involved from the level of the sixth rib to the ankles except for a few small patches. Associated with this was rheumatoid arthritis; the hips and knees were ankylosed, and there was marked limitation of motion of the ankles. Crawford gives the following description of acute plaques of morphea. They "usually commence with a definitely bright or dusky erythematous induration, which may be slightly elevated. . . . They are frequently multiple and enlarge rapidly in all directions, often fusing. . . . The advancing border is often slightly elevated and of a peculiar bluish red, while the interior of the plaque is flat and faintly pink or violaceous, finally assuming the color of ivory. The older portions resolve into thin, soft atrophied tissue with smaller scattered areas of residual induration which eventually atrophy."

The child had as possible sources of infection three carious teeth and large, infected tonsils, which were removed during the course of treatment. X-ray pictures of the hips showed a bony ridge on each side which extended from the femur to the acetabulum on the left side and to the inferior edge of the pubic bone on the right side. The hips and the knees and ankles were treated orthopedically so that within two years' time the child was able to walk with crutches and finally without aid. The article includes photographs of the lesions of the skin as observed in the acute stage and after cicatrization had taken place.

DULIN, Iowa City.

METALLIC RETENTION IN DERMATOLOGICAL CONDITIONS WITH REMARKS ON TREATMENT. BINFORD THRONE and C. N. MYERS, Arch. Pediat. **53**:8 (Jan.) 1936.

Sources of metallic retention are discussed. Contamination of food from spray residues and occupational contact appear to be the most important factors in chronic arsenic and lead poisoning. Examples are cited of retention of metal as the cause of pathologic conditions, and various associated dermatologic conditions are listed. A résumé of treatment is given.

WADDELL, University, Va.

IS THERE AN INCREASED SUSPENSION STABILITY OF THE ERYTHROCYTES IN ALLERGIC DISEASE? R. V. ELLIS, J. Allergy **7**:64 (Nov.) 1935.

The work presented seems to indicate an increased suspension stability of erythrocytes in allergic disease. This would be valuable in differentiating an infection of the sinuses or nose from an allergic condition in the nose.

Ellis feels that the accepted normal sedimentation rate for allergic disease was established without careful exclusion of minor allergic manifestations. She feels that more work needs to be done, with care to exclude those persons for whom even a history of allergy in the family may be obtained.

HOYER, Cincinnati.

INTRACUTANEOUS TESTS IN NORMAL INDIVIDUALS: AN ANALYSIS OF 150 SUBJECTS. MAX H. GROW and NATHAN B. HERMAN, J. Allergy **7**:108 (Jan.) 1936.

Intracutaneous tests were made with thirteen different allergens of varying strengths. One hundred and ten patients had no history of any allergic manifestation. Eighty-three, or 55.5 per cent, reacted positively to one or more of the allergens.

HOYER, Cincinnati.

AIR CLEANING AS AN AID TO THE TREATMENT OF HAY FEVER AND BRONCHIAL ASTHMA. LEO H. CRIEP and M. A. GREEN, J. Allergy **7**:120 (Jan.) 1936.

An electrostatic air-cleaning apparatus is described. It removes from the air coarse and fine solid particles, pollen, and chemicals in liquid or solid form. It does not remove vapors or gases. It has given symptomatic relief in a group of sixty-one patients suffering from hay fever, and from dust and pollen asthma.

HOYER, Cincinnati.

GASTRIC ACIDITY AND ACID THERAPY IN ALLERGY. M. LOVELESS, J. Allergy **7**: 203 (March) 1936.

Carefully controlled experiments were carried out on sixty-nine adults and sixty-nine children in the clinic for patients with allergy.

The results do not reveal any correlation between allergy and decrease in gastric acidity. There was but little allergic difference associated with difference in localities.

There are several factors which may contribute to the variation in the results of different workers: viz., the method of filtration, the choice of color end-points in titration, the presence of mucus in the gastric contents and the occurrence of an asthmatic attack near the time of extraction of the gastric contents.

The clinical response in the allergic patierts treated with hydrochloric acid was not impressive.

HOYER, Cincinnati.

KAPOK: ITS IMPORTANCE IN CLINICAL ALLERGY. H. C. WAGNER and F. M. RACKEMANN, J. Allergy **7**:224 (March) 1936.

New unused kapok is less apt to evoke positive skin reactions and to produce clinical symptoms than old used kapok. Age and use break the fibers, and dust forms. The active principle obtained from extracts of kapok is freely soluble in water, is of small molecular size and gives evidence of the presence of a nonprotein nitrogen and possibly of a polysaccharide. More of the substance is found in the old used kapok than in the new unused fibers.

HOYER, Cincinnati.

SOME PHYSIOLOGICAL FACTORS IN THE PRODUCTION OF THE ALLERGIC STATE, OR WHY ASTHMA? EVERETT B. POOLE, J. South Carolina M. A. **32**:9 (Jan.) 1936.

Poole gives a most interesting review of the antigen-antibody reactions. The common conditions in this disturbance are asthma, hay fever, urticaria and sensitivity to drugs. There are physiologic alteration of smooth muscle and a disturbance of the capillaries. He expresses the belief that the action of histamine on the end-fibers of the vagus in the lung produces the asthma.

The origin of the vagus is closely associated with the accessory sinuses, particularly the sphenoid and ethmoid, and with the turbinate bones. Operation in the regions near these structures is not advised except for polyps and associated conditions. Asthma as a familial condition is important, as more than half the patients had a record of allergic condition on the paternal or maternal side (more on the latter).

WESTON JR., Columbia, S. C.

THE TREATMENT OF SOME OF THE MORE COMMON SKIN DISORDERS IN INFANCY. C. G. WEIGAND, Nebraska State M. J. **21**:125 (April) 1936.

Attention is called to the fact that the infant has a delicate skin and needs constant care to keep it in a healthy condition. Too strong a soap is sometimes a factor in producing irritation of the skin. Impetigo, boils and abscesses may be superimposed on irritation of the skin. Cleanliness and dryness are essential. Impregnation of the diaper with mercury bichloride or with boric acid solution is recommended to prevent diaper dermatitis. A bran or starch bath is used

for heat rash. For a dry scaly skin, olive oil is used after the bath. Severe "cradle cap" is treated with cold cream containing from 1 to 3 per cent salicylic acid applied once daily. For the treatment of infantile eczema, the reader is referred to Lewis Webb Hill's article on that subject. Impetigo is managed by the use of green soap, 2 to 5 per cent ammoniated mercury, and sometimes 5 per cent silver nitrate solution; ultraviolet rays and exposure to air are also adjuncts. The use of thyroid in ichthyosis is suggested. The treatment of nevi is referred to the dermatologist. In the management of any cutaneous disease, nourishment, fresh air, cod liver oil and sometimes rest in bed are essential.

HAMILTON, Omaha.

THERAPEUTIC VALUE OF CALCIUM SALTS IN SERUM SICKNESS. T. J. CURPHEY and S. SOLOMON, New England J. Med. **214**:150 (Jan. 23) 1936.

In a series of patients with pneumococcic lobar pneumonia in Bellevue Hospital in whom serum sickness developed following treatment with antipneumococcus serum, fifteen were given the usual treatment employing epinephrine, ephedrine, sedatives and local applications of calamine lotion with phenol, and fifteen alternate ones were given the same treatment plus calcium gluconate in sufficiently large doses by intravenous and intramuscular injection.

Judged by the fading of the rash, the first group required an average of five and four-tenths days for relief and the second group two and nine-tenths days.

Including all the other usual symptoms (itching, arthralgia, headaches, cramps, nausea, etc.), the first group required seven and one-tenth days for complete relief and the calcium-treated group only three and three-tenths days.

GENGENBACH, Denver.

RAGWEED (CONTACT) DERMATITIS: OBSERVATIONS IN FORTY-EIGHT CASES AND REPORT OF UNSUCCESSFUL ATTEMNTS AT DESENSITIZATION BY INJECTION OF SPECIFIC OIL. L. A. BRUNSTING and D. H. WILLIAMS, Proc. Staff Meet., Mayo Clin. **11**:192 (March 18) 1936.

Forty-eight patients are presented who had the typical syndrome of recurrent seasonal dermatitis in the fall owing to sensitivity to oil of ragweed. Positive reactions were obtained by the patch tests to short ragweed, burweed, marsh elder and western ragweed.

In nineteen of twenty-four cases in which desensitizing treatments with oil in varying amounts had been given, there was no relief of symptoms, as shown by relapse during the expected season of dermatitis in the fall of 1935. In only two cases was there no relapse.

MILLER, South Bend, Ind.

DIAGNOSTIC MEASURES IN ATOPIC INFANTILE ECZMA. HERBERT J. RINKEL, South. M. J. **29**:507 (May) 1936.

The diagnosis of the precipitating causes of atopic eczema is essentially that of food allergy. The possibility of allergy in any case of eczema cannot be eliminated until all the diagnostic measures have collectively indicated that there is no relation between the symptoms and the diet.

The accuracy of cutaneous testing is approximately 50 per cent in those cases in which there are cutaneous reactions, while 20 per cent of the patients with eczema do not give any reaction. The scratch method is superior to the intracutaneous method on a basis of specificity.

Elimination diets must be used with due regard to the botanical relationship of foods, since two of every five sensitizations are complete for the botanical food group.

Diet and symptom records in the author's hands have revealed twice as many causes of eczema as were revealed by cutaneous testing and represent a most valuable diagnostic measure. Clinical observation is a necessary procedure in every case as a check for all laboratory tests employed.

The leukopenic index is of distinct aid, since it may be used regardless of the clinical state of the eczema. Its accuracy has been found to be the same for eczema as for other types of food allergy, being approximately 84 per cent.

SCHLUTZ, Chicago.

IMPROVEMENT OCCURRING IN CASES OF CALCINOSIS UNIVERSALIS IN CHILDREN. F. PARKES WEBER, Brit. J. Dermat. **47**:400 (Oct.) 1935.

The author reports the occurrence of calcinosis universalis in three girls; diminution of the calcareous deposits was shown by roentgen examinations. The treatment included the use of iodides, a ketogenic diet and disodium phosphate.

WIEN, Chicago. [ARCH. DERMAT. & SYPH.]

FULGURATION AND DIATHERMY COAGULATION IN CERTAIN SUPERFICIAL CONDITIONS. C. H. C. DALTON, Brit. J. Phys. Med. **10**:134 (Dec.) 1935.

A technic is described and recommended as the method of choice for removal of warts, nevi, pigmented moles and sebaceous nodules.

HARTMAN, Cleveland.

ARTERIAL CALCIFICATION AND SUBCUTANEOUS CALCINOSIS IN A BOY AGED TWENTY MONTHS. J. H. SHELDON and W. SHELDON, Proc. Roy. Soc. Med. **29**:499 (March) 1936.

The family history and the previous history of the patient, as well as the results of physical examination and the notes on the progress of the disease are given in the report. Roentgen examination showed the epiphysial lines of the long bones densely calcified, the femoral and iliac arteries calcified, plaques of calcification present in the subcutaneous tissues around both knee joints, and two smaller plaques present just below the right elbow joint.

WILLIAMSON, New Orleans.

HEREDITARY AND FAMILIAL PALMAR AND PLANTAR KERATODERMA. G. BASCH, ABRAHAM and F. SIGUIER, Bull. Soc. franç. de dermat. et syph. **41**:945 (June) 1934.

A mother and daughter had keratoderma of the palms and soles, and the mother's grandfather, her father, a sister and a brother were similarly afflicted. The mother's basal metabolic rate was + 18 per cent; that of the daughter was + 10 per cent; the authors regard this as possible evidence that thyroid dysfunction is the cause of this disease.

GANDY, Houston, Texas. [ARCH. DERMAT. & SYPH.]

ABDOMINAL PAIN AS A MANIFESTATION OF SERUM SICKNESS. MICHAEL CARMINE, Bull. Soc. de pédiat. de Iasi **6**:39 (April-June) 1935.

Only rarely does severe abdominal pain occur with serum sickness. Two cases are reported. One patient, a girl of 6 years with cerebrospinal meningitis treated with antimeningococcus serum, had on the eighth day an urticarial eruption and three days later abdominal pain, which recurred in crises for twenty days. The second patient, a boy 11 years of age, had abdominal pain seventeen days after the administration of diphtheria antitoxin. He had at the same time a scarlatiniform eruption and pains in the joints. The abdominal pain persisted for fifteen days.

LESLIE, Evanston, Ill.

NEUROFIBROMATOSIS IN AN INFANT. L. BABONNEIX and LAUTMANN, Bull. Soc. de pédiat. de Paris **34**:151 (March) 1936.

A boy 9 months old died of bronchopneumonia. He had localized pigmented areas on the arms, a soft mass in the right buttock and an enormous hairy pig-

mented nevus extending over the entire diaper area and a little farther upward anteriorly and posteriorly. There was also spina bifida. There was no histologic confirmation of the diagnosis of neurofibromatosis.

BENJAMIN, Montreal, Canada.

DISSEMINATED LUPUS. L. BABONNEIX, R. RABUT and ROUÈCHE, Bull. Soc. de pédiat. de Paris **34**:152 (March) 1936.

A girl 11 years old had numerous lesions of the skin, which appeared first on the face and subsequently over the body. Material examined histologically showed the typical tubercle formations of lupus. The cutaneous reaction to tuberculin was negative.

BENJAMIN, Montreal, Canada.

NECROTIC PYODERMA IN THE COURSE OF PROLONGED INFECTION. L. RIBADEAU-DUMAS and LE MELLETIER, Bull. Soc. de pédiat. de Paris **34**:175 (March) 1936.

Two boys, 5 and 6½ months old, respectively, had protracted infection, especially of the middle ear. Numerous necrotic skin lesions developed, which were thought to have an embolic origin.

BENJAMIN, Montreal, Canada.

PROGRESSIVE LIPODYSTROPHY. H. ROGER, J. ALLIEZ and J. E. PAILLAS, Rev. franç. d'endocrinol. **13**:443 (Dec.) 1935.

Progressive lipodystrophy was known to the prehistoric cave-dweller, as Guiart has recently reproduced an ivory figurine with lipodystrophic features. Ameline and Quercy expressed the belief that Pharaoh Amenophis IV suffered from the same disease. Although credit must be given to Morgagni for drawing attention to this condition, the first accurate descriptions were made by Barraquer and Simons, by whose names the disease is now known. In addition to the classic features described by Simons, others have noted vasomotor disturbances, mental manifestations in the form of anxiety states, polyuria and glycosuria and bony deformities. The authors mention anatomic changes, such as: atrophy of the hypophysis, in the case of Zalla; ovarian lesions, in the case of Laignel-Lavastine; increase in the chromophilic and eosinophilic cells of the hypophysis, noted by Marburg, and slight increase in the fat tissue and pigment cells of the adrenal cortex, in the case of Hussler. Comparing this condition with Cushing's syndrome, which presents the opposite picture, they suggest the possibility of opposite factors operating in the two entities. They realize, however, that this theory is highly speculative, since numerous experiments on the hypophysis failed to reproduce the condition and administration of pituitary gland preparations has not influenced the course of the disease.

They also consider the possibility of involvement of the central nervous system proper. In this connection they mention the theory advanced by Meige of a congenital or acquired defect in the segmental trophic centers of the spinal cord or in the sympathetic centers as an explanation of the metameric distribution of the atrophy. They see another possibility in involvement of the metabolic regulatory centers in the diencephalon. They admit, however, that such a theory is not tenable.

They report a typical case of progressive lipodystrophy and believe that they were dealing with pronounced involvement of the autonomic-endocrine systems; they invoke the following points in favor of this possibility: The alteration in the vascular systems is evidence of hypophysial dysfunction, as the same condition was present in the case of Long and Bickel, in which the pituitary body showed changes. The disturbance in sugar metabolism is evidence of autonomic involvement, while the results of the interferometric tests speak in favor of widespread glandular dysfunction. They discuss the paradoxical association of chronic arthritis

and pronounced hypotonia in their case and suggest that fatty atrophy, arthritis and hypotonia are probably all of the same origin. They believe that diencephalic involvement could explain the metabolic, arthritic and tonic disturbances, and in support of this assumption they invoke the striatal changes observed in the case of lipodystrophy of encephalitic origin reported by Sarbo.

NOTKIN, Poughkeepsie, N. Y. [ARCH. NEUROL. & PSYCHIAT.]

ATTENUATED FORMS OF ACRODYNIA. E. LEENHARDT, J. BOUCOMONT and R. LAFON, Rev. franç. de pédiat. **11**:689, 1935.

Leenhardt, Boucomont and Lafon report cases of their own and review cases from the literature, which are probably instances of mild forms of acrodynia. The most constant symptoms are loss of weight and loss of appetite, persisting over a long period. The associated findings suggesting acrodynia are cold, moist, slightly red fingers or toes (one or more), evidence of itching of the body as revealed by scratches, tachycardia (the pulse rate usually being 120 beats per minute) and hypertension. Examination with the capillaroscope reveals dilatation of the subpapillary plexus and normal, increased or only slightly diminished rapidity of circulation, never greatly diminished. These findings are similar to those reported by the authors in cases of acute acrodynia. They feel that the recognition of mild forms of acrodynia may lead to a better understanding of the epidemiology of this condition.

LESLIE, Evanston, Ill.

A CLINICAL STATISTICAL CONTRIBUTION TO THE STUDY OF THE CUTANEOUS MANIFESTATIONS OF THE EXUDATIVE DIATHESIS IN THE BREAST-FED INFANT AND ITS TREATMENT BY GIVING THE MOTHER A LOW CHLORIDE DIET. R. PACHIOLI, Riv. di clin. pediat. **34**:219 (March) 1936.

Exudate diathesis in the first three months is of one of two types. It may be a seborrheic dermatitis or an erythroderma with desquamation. The latter is the more serious condition, with a mortality, according to different authors, varying between 26 and 88 per cent. After the first three months of life the exudative diathesis may develop into infantile eczema.

A series of seventy-eight cases of exudative diathesis were observed in the pediatric clinic at Bologna. Most of the patients had erythroderma; fifty-one were treated by various therapeutic procedures, such as the administration of epinephrine, thyroid, calcium, digestive ferments, soy bean or insulin. The mortality was 38.5 per cent. The remaining twenty-seven were treated by giving the mother a low salt diet; the mortality was 9.5 per cent; beneficial results were manifest in from seven to sixteen days after the beginning of treatment, and the maximum benefit was obtained by the twenty-fifth day.

The diet of the mother must be carried out with scrupulous strictness and with especial care that no medicine containing sodium chloride or any salts of sodium or potassium is taken. The lower chloride diet for the mother did not lead to improvement of infantile eczema in children over 3 months of age.

HIGGINS, Boston.

RARE FORMS OF NEVI IN CHILDHOOD. R. STEINDLER, Arch. f. Kinderh. **107**:237, 1936.

Two cases of unusual forms of nevi and two cases of mongolian spots on the scalp are reported.

CRANE, Chicago.

UNUSUAL ERUPTION IN AN INFANT CAUSED BY PERNOCTON. R. FRÜHWALD, Dermat. Wchnschr. **101**:1424 (Nov. 16) 1935.

In a 4 week old infant there developed a tuberous and bullous eruption involving chiefly the face but extending also to the trunk. Shortly after the birth of the

child the mother had been given several injections of pernocton (sodium salt of secondary butylbetabromallylbarbiturate). It was considered that the infant's eruption was a bromoderma due to bromide in the mother's milk.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

NEW FINDINGS CONCERNING FURUNCLES AND FURUNCULOSIS. M. M. LEWIN, Dermat. Ztschr. **71**:197 (June) 1935.

Lewin obtained cultures of staphylococci from furuncles of patients with a single furuncle and with furunculosis, from apparently normal skin of patients with furunculosis, from patients with weeping dermatoses, and from persons without cutaneous lesions. The virulence of these cultures was determined by intracutaneous injections into the skin of rabbits, the reactions being graded according to their severity and duration. Cultures obtained from the furuncles themselves were most virulent, in a number of instances causing necrotic and pustular reactions. Cultures from normal skin of patients with furunculosis and from areas of weeping dermatoses were somewhat less virulent, and those from patients without cutaneous conditions were only slightly virulent. The author concludes that a virulent strain of staphylococci rather than a reduced resistance is responsible for the development of furuncles.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

POISONING BY SULFUR DURING TREATMENT OF SCABIES. S. NITTO, Jap. J. Dermat. & Urol. **38**:434 (Sept.) 1935.

Nitto treated a mother and two of her children for scabies, using percutaneous inunctions of a 10 per cent purethan solution (an organic sulfur combination) in olive oil. The same night, at home, severe vomiting, diarrhea and fever (39.7 C. [103.46 F.] developed in the mother; the itching, however, disappeared. After a day the vomiting and diarrhea also subsided, but the temperature remained 39.1 C. (102.28 F.), and slight edema about the eyes persisted. All the symptoms returned after inunction with mitigal (a sulfur compound). It is believed that the general symptoms were due to percutaneous resorption of the sulfur constituents of these preparations.

J. W. BRENNAN, Chicago. [ARCH. DERMAT. & SYPH.]

ECZEMATOUS CHANGES IN THE SKIN AND FAT METABOLISM. T. OZAKI, Jap. J. Dermat. & Urol. **38**:771 (Nov.) 1935.

Ozaki studied the total fatty acids, phosphatides (lecithin) and total cholesterol content of the skin in relation to experimental dermatitis produced by croton oil. The total fatty acids were extracted with ether and alcohol, saponified with sodium hydroxide and weighed dry. The phosphorus content of the lecithin substances, ashed with sulfuric acid and fuming nitric acid, was determined by multiplying the theoretical factor 0.054 by the amount of four hundredths-normal sodium hydroxide required to dissolve a precipitate of ammonium phosphomolybate. For determination of the cholesterol content the free cholesterol was weighed as a digitonin precipitate, the residual cholesterol ester being then saponified with sodium alcoholate and precipitated and weighed as described for phosphorus. The methods used are those described in Takata's "Biochemical Analysis" (Shōkwagaki Bunseki, 1927, p. 610), the digitonin method being a modification of the Windaus method (*Ztschr. f. physiol. Chem.* **65**:110, 1910).

During the acute stage of the croton oil dermatitis in the rabbit the amounts of total fatty acids, phosphatides and cholesterol diminish markedly; they rise to abnormally high values during the subacute stage (nineteenth day) and finally sink gradually back to normal. Tables showing the variations of each constituent in milligrams per hundred grams of skin accompany the article.

The conclusion is that experimental dermatitis exerts an influence on the metabolism of fats.

J. W. BRENNAN, Chicago. [ARCH. DERMAT. & SYPH.]

PATHOGENESIS OF IMPETIGO CONTAGIOSA ALBOSTAPHYLOGENES (DOHI). H. ASANO, Jap. J. Dermat. & Urol. **38**:792 (Nov.) 1935.

A vesicular eruption consisting of single or multiple translucent, flaccid vesicles from the size of a millet seed to that of a cherry with a meager surrounding general inflammatory reaction or none is frequently encountered during the warm, humid months in Japan. It has been studied by the Dohis and others and ascribed to Staphylococcus albus. In the relatively few cases in which Staphylococcus aureus has been the organism encountered it has been dismissed from consideration as merely a secondary invader or part of a mixed infection.

Asano, however, secured Staph. aureus in pure culture in 21.4 per cent of a group of cases of this disorder. By means of parallel studies of Staph. albus and Staph. aureus as to biologic characteristics (coagulation of milk, fermentation of sugars, hemolytic power, culture on crystal violet mediums, agglutination reaction, resistance to acid and to heat, behavior toward antiseptics, such as acriflavine hydrochloride, an acridine derivative and glycerin, toxicity when injected intraperitoneally into rats and toxicity for the skin of rabbits, of guinea-pigs and of puppies) and especially by observation of the results of intracutaneous injection into the skin of the forearms of nurslings she arrived at the conclusion that in certain cases Staph. aureus may be the sole pathogenic agent. Therefore, she considers the name impetigo contagiosa albostaphylogenes (Dohi) to be inappropriate and proposes in its stead the name impetigo albo-aureostaphylogenes or impetigo staphylogenes infantum.

Asano found the biologic behavior of the staphylococci of the normal flora of the skin to be identical with that of the staphylococcus causing impetigo. She believes that the reason that these organisms at times invade the subepidermal layers of the skin, producing the typical superficial vesicular lesion of impetigo, may be found in the difficulty in immediately getting rid of the sweat by evaporation. During the late part of the summer humid sultriness prevails in the region of the city of Osaka, where Osana is doing her work, and she believes that alkalinization (formation of ammonia) due to decomposition of the sweat and diminution of the sterilizing effect of drying are favorable to the growth of the staphylococcus. To these climatic factors are added the ease with which minute abrasions are produced in soggy, wet skin and the delicate make-up of the skin of nursling children.

Asano believes that the reason for the scarcity of this condition in nurslings before the fourth month of life lies in the fact that the sweat glands are not fully developed before that time.

J. W. BRENNAN, Chicago. [ARCH. DERMAT. & SYPH.]

BLISTER FORMATION FOLLOWING EXTERNAL APPLICATION OF PETROLEUM. M. J. MAZEE-DEINUM, Maandschr. v. kindergeneesk. **5**:267 (March) 1936.

This is a description of three cases of formation of blisters after application of petroleum on the scalp. The blisters appeared at places where no petroleum was applied.

VAN CREVELD, Amsterdam, Netherlands.

Surgery and Orthopedics

BITE WOUNDS. E. HUDACSEK, Beitr. z. klin. Chir. **161**:337, 1935.

During 1934 Hudacsek collected 781 cases of bite wounds (678 cases due to dog bites and the remainder, except a small number due to human bites, divided up among other animals).

He had this opportunity to treat such a large number of bite wounds because all those seen at the Pasteur Institute which necessitated surgical intervention were referred to him.

Wounds of this type heal much more slowly than any other kind, sometimes taking five times as long. No tetanus was observed in any of the cases. Some of

the wounds could be considered practically sterile (because of bactericidal property of saliva?). In a great number of the cases it was found much more feasible to excise wound areas, this procedure resulting in primary healing.

RUBIN, Boston.

THE FEEDING OF INFANTS AFTER OPERATIONS. E. GYÖRGY, Orvosi hetil. **80**:100 (Feb. 1) 1936.

After operations on infants the feeding of the infants is very important, because an operation plays the rôle of trauma in the organism of an infant; furthermore, infants stand the loss of blood very badly, and narcosis is not altogether harmless for them. Before an operation without narcosis, one feeding should be omitted, and only tea should be given for six hours after the operation. The feeding should be begun in little portions, but tea can be given abundantly. For the first two days after the operation the best feeding is mother's milk. When an operation is to be accompanied with narcosis, the infant should receive nothing for six hours before the operation, and even tea can be given only six hours after the operation. Feeding begins eighteen hours after the operation with small quantities of breast milk. These infants should be treated for from three to four days as infants with dehydration and acidosis.

GÖTTCHE, Budapest, Hungary.

Teeth and Dentistry

FLUORIDE TOXICOSIS: A PUBLIC HEALTH PROBLEM. M. C. SMITH, Am. J. Pub. Health **25**:696 (June) 1935.

Mottling of the dental enamel due to fluoride in water has been found in certain sections of twenty-four states; it is more prevalent in the arid states of the Southwest. The fluoride content of water varies from 1 to 6 parts per million. One part per million will cause mottling if it comes in contact with the tooth during the period of the formation of enamel, but it will not do so after the tooth is fully erupted. Only permanent teeth are affected, unless the fluoride content of the water is unusually high. Increased intakes of calcium and vitamin D do not prevent the action of fluoride on teeth. Experiments on rats suggest that the dentin of the adult tooth may suffer from ingestion of fluoride. Fluoride compounds are commonly used to spray vegetables, and carefully washed vegetables still contain sufficient fluoride to be dangerous to persons who eat them. The use of fluoride for spraying should be discontinued.

MCBRYDE, Durham, N. C.

RÔLE OF HEREDITY IN DISEASE. M. T. MACKLIN, Medicine **14**:1 (Feb.) 1935.

Macklin reviews the rôle of heredity in disease in the light of modern genetics. The review is comprehensive. It does not lend itself to abstracting. His view is expressed in the closing sentences of the article: "converging streams of germ plasm with their varying potentialities have met to make him what he is; how he reacts to his environment, what disabilities he meets along the way, what form death assumes when finally it removes him from the scene are largely determined by his heritage.

MCBRYDE, Durham, N. C.

RECENT PROGRESS IN PEDIATRICS. M. VARGAS, Med. de los niños **37**:72 (March) 1936.

Among the contributions to pediatrics in recent years the following are noteworthy: 1. Children whose growth is retarded show improvement with injections of extracts of the anterior lobe of the pituitary gland; extracts of the thymus gland improve growth and are useful in treating cryptorchidism and adiposogenital dystrophies. 2. Vitamin A in the form of carotene has not given the expected

results in anemic infants; orange juice or tomato juice, cod liver oil and carotene must be given. No appreciable direct anti-infective action results from vitamin therapy. There is an indirect benefit from the general improvement of the patient's resistance. 3. Changes in climate, temperature and moisture such as are encountered by children in moving from rural to urban centers have a definite influence on health and especially on the incidence of gastro-intestinal disturbances and rheumatism. 4. Patients with acrodynia show improvement on treatment with methenamine and acetylcholine. 5. Children who have been immunized against diphtheria may have the disease in a benign form. In immunized children the mortality from diphtheria is 4.8 per cent; in the nonimmunized it is 11 per cent. 6. Rhinovaccination against diphtheria may be carried out by the use of 0.25 Gm. of a paste made by evaporating a mixture of antitoxin and 10 per cent almond oil. 7. Strychnine in doses of 0.5 mg. per kilogram of body weight each day may be given in cases of malignant diphtheria to prevent postdiphtheritic paralysis. 8. Rare complications of diphtheria are: encephalitis, hemiplegia with aphasia and facial paralysis. In severe diphtheria serum should be given up to 60,000 units. 9. Acute abdominal pain, vomiting and meningeal symptoms have been reported as the initial signs of acute articular rheumatism; these are followed by pericardial friction and later by mitral insufficiency. 10. Excellent results are reported from the use of convalescent scarlet fever serum in doses of 30 cc. daily. 11. Gautier has shown that the increase of urea in the blood during scarlet fever has no relation to the nephritis of scarlet fever. Urea may increase to from 40 to 65 mg. per hundred cubic centimeters of blood and return to normal within fifteen days. 12. The ninth case of pneumococcic meningitis in the new-born to be recorded in pediatric literature is reported by Coppolino and Ganone; the onset occurred on the second day of life. 13. Progress has been made in the prevention of poliomyelitis through the efforts of Kolmer and Rulle, also those of Brodie and Park. Kolmer and Rulle prepared a vaccine, using sodium ricinoleate and the virus obtained from the spinal cord of a monkey. This was used in twenty-five children between the ages of 8 months and 15 years at Temple University Hospital, with good results. The blood of these children showed considerable quantities of antibodies. Brodie and Park prepared a similar vaccine, using virus and solution of formaldehyde U.S.P. (1:10), and found it efficacious in an epidemic of poliomyelitis in California. Paulis considers poliomyelitis a manifestation of tuberculosis of the nervous system. He used the åntialpha vaccine of Ferrán as a prophylatic, and during ten years' experimentation with this he has not seen a case of poliomyelitis in a child who has received it. 14. The new treatment of tetanus consists in giving antitetanic serum subcutaneously and intraspinally and frequently using chloroform. 15. Several children given BCG vaccine have been known to succumb several years later to tuberculous meningitis. However, their cases have not been studied sufficiently to be reasonably sure of the origin of the infection.

DWYER, Kansas City, Mo.

A COMPARATIVE STUDY OF THE TEETH IN CHILDREN AT A DAY NURSERY AND AT A CHILDREN'S HOME IN OSLO. A. COLLETT, Tidskr. f. d. norske laegeforen., no. 22, 1935.

The children were aged from 3 to 7. In the children's home they got a very simple and cheap food on which they throve satisfactorily (raw fruit after each meal, 1 dessert-spoonful of cod liver oil daily, boiled vegetables and potatoes, cocoa butter, and sugar in small quantities; no other sweets; bread made of 50 per cent unbolted meal; small quantities of meat and fish four times a week). There was no brushing of the teeth. In the day nursery the children get a cooked dish, and one third of a liter of whole milk is added to the sandwiches which they bring from their own homes. They live as the usual Oslo labor class lives; i. e., they receive much sugar and a great quantity of sweets and mostly soft bread and cakes of bolted flour. Brushing of the the teeth is practiced daily. A comparison of the teeth of these two different groups of children shows that they

are much more decayed in the last group. Collett is of the opinion that the decay of the teeth presents a question of diet and that natural food protects the teeth, while denatured, refined food, especially industrial sugar and bolted flour, ruins them.

WALLGREN, Gothenburg, Sweden.

Miscellaneous

"KNOPPIE-SPIDER" BITE. M. H. FINLAYSON, South Africa M. J. **10**:43 (Jan. 25) 1936.

Cases of spider bite followed by death, due to spiders of the genus Lactrodectus, have been reported in the United States, Australia, New Zealand and South America. Specimens of Lactrodectus obtained in Cape Town have been identified as Lactrodectus geometricus. The "knoppie-spiders" obtained from the Graafwater, Piquetberg and Malmesbury areas have been identified as Lactrodectus concinnus and Lactrodectus indistinctus. L. geometricus and L. concinnus are found in outhouses and about the windows and doors of human habitations; Lactrodectus indistinctus lives only in the cornfields and on the veld. The characteristic features of these species are described.

"The symptoms following bites by a 'knoppie-spider' may vary in different individuals, but in almost all cases severe cramp-like pain is experienced, in the chest or abdomen. Frequently abdominal rigidity is observed, and in the majority of cases profuse perspiration is noted and salivation may be marked. The temperature may be subnormal, but rapidly rises to 102° or 103° F. The reflexes are overactive and the patient is often cyanosed. In some cases nausea and vomiting are present, in others difficulty in breathing. Death may ensue from heart failure or respiratory failure. Both in man and animals the symptoms are neurotoxic, and in this respect resemble those produced by Cape cobra venom."

Experimental studies of extracts of the heads of the various species showed that the lethal dose of an extract of L. indistinctus for mice is from two to four times the lethal dose of cobra venom, that extracts of L. geometricus and L. concinnus are much less toxic than an extract of L. indistinctus and that L. indistinctus antiserum completely neutralizes not only the homologous venom but also the venom of L. geometricus and of L. concinnus. None of the extracts from these spiders neutralized Cape cobra and puff-adder antivenins.

For the treatment of "knoppie-spider" bite the antiserum for L. indistinctus seems to be the most useful. Cape cobra and puff-adder antivenins are certainly useless. At the Los Angeles General Hospital convalescent serum is used. Because of the possibility of tetanus as a complication of spider bite the use of tetanus antitoxin should be considered in all cases. It should not be difficult for serum manufacturers to produce an antiserum against L. indistinctus, incorporating sufficient tetanus antitoxin to provide against possible tetanus infection.

GONCE, Madison, Wis.

PHARMACOLOGY AND PHARMACODYNAMICS OF CHILDHOOD: V. ANTIPYRETICS (ANIMAL EXPERIMENTS). S. BLAZSÓ, Arch. f. Kinderh. **104**:200 (March 29) 1935.

The tolerance of rats during the period of growth to four antipyretics was studied by a uniform technic. It was established that the tolerance of growing rats for aminopyrine is much greater than that of adult animals. The same is true with regard to antipyrine or sodium salicylate for the first two weeks of life, but at the end of this period the increased tolerance is changed to hypersensitivity. To quinine hydrochloride the reactions are the reverse of those described: During the first twelve days of life the rats are relatively hypersensitive, while from twelve days to maturity they have a strikingly high tolerance.

CRANE, Chicago.

PHARMACOLOGY AND PHARMACODYNAMICS OF CHILDHOOD. VI. ANTIPYRETICS (CLINICAL SECTION). G. PETRÁNYI, Arch. f. Kinderh. **104**:225 (March 29) 1935.

Clinical study of the effect of antipyretics on fevers of various types in children shows that the antipyretics may be divided into four groups: (1) aminopyrine, (2) antipyrine, acetophenetidin, (3) quinine, (4) salicylate derivatives. The first group is capable of combating severe fevers; the fourth group reduces only milk fevers; the other two groups fall in between, in the order in which they are listed. No bad effects were obtained from energetic antipyresis either in regard to the course of the disease or in regard to unpleasant associated symptoms.

CRANE, Chicago.

TOLERANCE TO CODEINE DURING CHILDHOOD. O. CHIARI, Arch. f. Kinderh. **105**: 223 (July 16) 1935.

A series of experiments showed children to be more tolerant of codeine than are adults. Children weighing 20 Kg. or less can take a dose of 3 mg. per kilogram once a day, but children whose weight is 30 Kg. do not tolerate a proportionate dose so well. Since the toxic dose of codeine is relatively so high, it is to be assumed that the therapeutic dose should not be so low as that previously used.

CRANE, Chicago.

PHARMACOLOGY AND PHARMACODYNAMICS OF CHILDHOOD: VII. EXCRETION OF OPTOCHIN. S. BLAZSÓ and T. VARGA, Arch. f. Kinderh. **105**:234 (July 16) 1935.

The investigations reported reveal previously unknown laws of the excretion of optochin: 1. The time of initial appearance and the duration of excretion and the proportion excreted vary according to the size of the single dose. 2. If the dosage is repeated daily or every second day, the excretion varies from dose to dose even though the same dose is used—the excretion begins earlier and earlier and continues for a longer period, and the proportion excreted is continuously greater. 3. Much speaks for the theory that the cause of this variation is to be sought in the change in the saturation of the reticulo-endothelial system with repeated dosage.

CRANE, Chicago.

EXPERIMENTAL STUDIES OF THE TOXIC ACTION OF THE SPORES OF MAIZE RUST (USTILAGO MAIDIS). B. DRAGIŠIĆ and B. VARIĆAK, Arch. f. Kinderh. **107**: 140, 1936.

The authors' experimental results indicate that Ustilago maidis from Jugoslavia exerts a striking toxic effect, lending further support to Mayerhof's clinical portrayal of ustilaginismus. The authors succeeded in producing in animals a clinical picture like that of the acrodynia one is accustomed to see in children.

Findings very similar to those in experimental ergot poisoning were obtained but with the difference that with Ustilago maidis clonic and tonic convulsions were produced, which up to the present have never been produced in experimental ergot poisoning.

From the similar toxic actions of the spores of maize rust and the spores of ergot it is evident that in Ustilago maidis from Jugoslavia ergotamin-like substances are present, and, indeed, not in such small amounts as some investigators found in other material, but in quantities such as to justify the authors in concluding on the basis of their experimental studies that Ustilago maidis possesses a stronger toxic action than ergot itself.

CRANE, Chicago.

PHARMACOLOGY AND PHARMACODYNAMICS OF CHILDHOOD: IX. THE EFFECT OF REMEDIES FOR FEVER ON THE BASAL METABOLISM OF THE FEVERISH CHILD. G. PETRÁNYI and A. BÁNOS, Arch. f. Kinderh. **107**:220, 1936.

The effect of antipyretics on the basal metabolism of typhoid patients with high fever was tested. The increased metabolism which exists during fever was reduced almost to normal by successful antipyresis, but there was no drop if the antipyretic was ineffectual in lowering the fever. After the metabolism has become normal during convalescence it is not influenced by antipyretics. One may conclude that antipyretics not only allay the unpleasant symptoms accompanying fever but, by reducing the pathologically increased metabolism, exercise a direct protective influence on the feverish patient.

CRANE, Chicago.

NICOTINE POISONING IN AN INFANT. I. GREINER, Orvosi hetil. **80**: 59 (Jan. 18) 1936.

A 3 week old breast-fed infant suddenly began to vomit and kept vomiting intermittently. He drew up his legs; his pupils grew very small; his tongue became red. Poisoning was suspected, but because neither the mother nor the child had received any drugs, Greiner thought of the possibility of nicotine poisoning, as the mother smoked from thirty to forty cigarets daily. The mother was stopped from smoking, and the child continued to be fed her milk. In a few days he was well. Nicotine may appear in a mother's milk if she smokes more than fifteen cigarets daily and may cause toxic symptoms. A nursing mother should be prohibited from smoking or should be limited to six cigarets daily.

GÖTTCHE, Budapest, Hungary.

FOSTER INFANTS OF COPENHAGEN. POUL HERTZ, Nord. hyg. tidskr. **16**:311, 1935.

Infants which, according to the social law, are supervised by the community are visited by trained nurses every tenth day during their first half year of life and every fourteenth day during their second half year. In 1930-1933 there were supervised in this manner 4,901 infants. Of these, 6.8 per cent were born with a weight of 2,500 Gm. or less at birth. Of the infants of unmarried mothers, 85 per cent were breast fed; 5 per cent were bottle fed, and 10 per cent received a mixed feeding during their stay at the lying-in hospital. At the age of 2 months 63 per cent were still partially or exclusively breast fed; at the age of 4 months, 47 per cent, and at the age of 6 months, 35 per cent. Among the infants of married mothers breast feeding was still commoner: At the age of 6 months 55 per cent of these infants were still breast fed. Hertz finds that breast feeding is much more used now than at a period twenty years earlier. The mother, when necessary, receives economic support from the community during the first six weeks after the delivery of her child and gets 1 liter of milk daily if she feeds her own child. As to morbidity, Hertz reports a very striking result: No less than 61 per cent of all these infants have been quite healthy during the first year of life. In 133 the death rate of legitimate infants was 5.4 per cent.

WALLGREN, Gothenburg, Sweden.

RESEARCH ON TWINS. P. A. VOÛTE, Maandschr. v. kindergeneesk. **5**:202 (Feb.) 1936.

A description is given of the two methods by which monozygotic and dizygotic twins can be distinguished. In an investigation of a large series of cases of twin births in the obstetric clinics of Utrecht and Rotterdam it was statistically proved that about 30 per cent of all monozygotic twins are born in two separate chorions. So by the obstetric method it is possible to diagnose only those monozygotic twins that are born in one chorion. Stress is laid on the great importance of this fact.

Though limited in its use, the obstetric method should not be overlooked, because it is an objective one. This cannot be said of the second, the so-called polysymptomatic or resemblance method. As there is no proof of an obligatory likeness of monozygotic twins, it is to be understood that sometimes doubt as to the diagnosis will remain. This is demonstrated by two cases of monozygotic (single chorion) twins, one having a harelip and the other totally free from the anomaly, though harelip was hereditary in both families. These observations cast a strange light on the possibilities concealed in two of the same genotypes; an acceptable explanation of the divergency cannot be given. As to the research work on twins, it seems possible to follow two lines of investigation: (1) comparison of series of monozygotic and dizygotic twins, and (2) investigation of monozygotic twins which live in different environmental circumstances. These principal methods of research are discussed briefly and illustrated by examples.

VAN CREVELD, Amsterdam, Netherlands.

Society Transactions

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

Ann Arbor, Mich., Oct. 30 and 31, 1936

SAMUEL J. LEVIN, M.D., *President*

D. MURRAY COWIE, M.D., *Secretary-Treasurer*

TRICHOPHYTIDS IN RELATION TO ECZEMA. DR. SAMUEL J. LEVIN and DR. G. WARREN HYDE, Detroit.

During the past few years a great deal of interest has developed regarding the subject of sensitivity to Trichophyton. The conception initiated abroad by Block and Jadassohn that cutaneous hypersensitivity to fungi exists is now widely accepted. Sulzberger and Wise reported the occurrence of hypersensitivity to Trichophyton in cases of dermatophytosis. Numerous reports have confirmed this point of view and have emphasized the importance of the dermal manifestations of hypersensitivity to fungi. The term trichophytids has been used to describe the cutaneous manifestations of hypersensitivity to Trichophyton.

The recognition and the treatment of hypersensitivity to Trichophyton, particularly that occurring with chronic eczema, are reported. The materials used for testing were an American oidiomycin and trichophytin and a heated Brazilian trichophytin said to contain over 300 strains of fungi. Intradermal tests were done in cases in which sensitivity was suspected. A positive reaction appeared in from twenty-four to forty-eight hours as an area of redness and induration resembling a positive reaction to tuberculin. Occasionally an immediate wheal-like reaction occurred, which we considered atypical but probably of diagnostic importance. It may have been due to one of the by-products of the fungus culture or to the culture medium rather than to a specific hypersensitivity to the fungus.

In cases of infantile eczema no definite positive reactions were obtained. Positive reactions were obtained in many cases of chronic eczema in older children and in adults. Complete intradermal tests were made in these cases. In many, prior to the test for sensitivity to fungi only partial relief was obtained by the elimination of factors eliciting positive cutaneous reactions. Treatment of the patients by desensitization to specific fungi, in conjunction with the elimination of other specific allergens, resulted in considerably better results and in a few complete cures. The American extract containing both monilias and trichophytons was injected intradermally two or three times a week. As the delayed tuberculin type of reaction diminished under treatment, the amount injected was increased by more frequent injections of more concentrated solutions. The Brazilian trichophytin vaccine caused no severe reactions. It was given subcutaneously two or three times a week in gradually increasing doses until a total of ten or more injections had been given. Once clinical cure has occurred, treatment should not be stopped. Sensitization with fungus extracts is similar to desensitization with pollen extracts. It may be necessary to continue with a maintenance dose of the extract at intervals of three or four weeks for a year or more to prevent relapses. Cutaneous hypersensitivity is decreased in most instances. An illustrative case report follows.

Atypical and easily misleading symptoms occurred in a boy of 12. He had been subject to severe pruritic vesicular dermatitis of the arms and legs for five consecutive years between February and May; the condition persisted for from six to twelve weeks. With each attack, typical allergic rhinitis developed. The cutaneous condition had been considered by dermatologists to be an infection due

to a fungus. Because of the seasonal recurrence and the allergic manifestations, allergy to tree pollen was suspected. Intradermal tests with tree pollen gave negative results. Both American and Brazilian trichophytin caused strongly positive reactions. After two treatments with the Brazilian extract the skin almost completely cleared and the nasal condition disappeared. We treated about 40 persons with trichophyton extracts, the results being good in 40 per cent. Most of these patients were under observation for about a year, not long enough for definite conclusions. The percentage of good results in the treatment of infections due to Trichophyton has been increased by the cooperation of the allergist and the dermatologist.

AGE AND RESISTANCE TO TUBERCULOSIS. DR. CLEMENT A. SMITH, Boston.

Of some 300 deaths due to tuberculosis at the Children's Hospital and the Infants' Hospital in eleven years, about 25 per cent occurred in the first year of life, 30 per cent in the second year and 16 per cent in the third. None of the next five years contributed over 8 per cent of the total, and none of the four years between the ages of 8 and 12, more than 1 or 2 per cent. I think it is evident that one must fear tuberculosis particularly in the early years of childhood and most of all in infancy.

Babies have no acquired immunity because of the absence of widespread tuberculous infection at younger ages. They are naturally more intimately handled and cared for than older children, and opportunity for infection due to massive contact is greater. Little children are weak and small and have no resistance to infection.

The more closely one observes a group of tuberculous babies, however, the more one is impressed with the amount of resistance they have to the disease itself. Numerous infants with positive reactions to tuberculin remain well; large amounts of pulmonary exudate are found accidentally in healthy-looking babies and resolve progressively and steadily, and occasionally an infant with miliary tuberculosis survives.

It is impossible to prove this clinical impression by clinical experiment. My co-workers and I are attempting to put it to the test of investigation with animals. The most important earlier investigations are those of Krause and of Wallgren. Krause found that young guinea-pigs showed local changes after inoculation which indicated considerable resistance. Wallgren found that very young rabbits and old rabbits tended to survive longer than adolescent rabbits after all had been inoculated with tubercle bacilli in doses proportionate to their weight.

We are now conducting similar experiments. Our data are presented as a report of progress rather than as a set of conclusions; so far the results seem of some interest. Our plan has been to inoculate groups of rabbits of varying ages intravenously with a suspension of virulent bovine tubercle bacilli, to measure their survival time and to determine by autopsy the extent and the type of tuberculous reaction present.

The first groups of rabbits inoculated were 5 litter mates aged 3 weeks, averaging 350 Gm.; 5 litter mates aged 7 weeks, averaging 1,350 Gm., and 2 nonrelated adults averaging 2,400 Gm. The average survival of the youngest rabbits was eighty-five days; of the middle group, thirty-four days, and of the oldest, fifty-six days. The groups behaved with a fair degree of uniformity.

Two weeks later a second experiment was begun. Because the suspension had stood for two weeks, a slightly larger dose was given, 0.075 mg. per kilogram instead of 0.05 mg. per kilogram. There were 2 groups, 4 litter mates 17 days old, averaging 215 Gm., and 3 well grown animals, averaging 1,850 Gm. Again the baby rabbits survived longer—longer in fact than any other group in either experiment—an average of one hundred and fifty-five days, as against ninety-two days for the 3 older rabbits.

Two valid objections may be raised to this work: that our material is small and that we present merely results due to variations in the dose. The first is partially answered by the uniformity of behavior of our several groups, and the

second, by the short survival of the group receiving the medium doses as compared with that of the groups receiving the smallest and the largest doses.

DISCUSSION

DR. D. MURRAY COWIE, Ann Arbor, Mich.: How soon after inoculation could a positive reaction to tuberculin be demonstrated?

DR. CLEMENT A. SMITH, Boston: All reactions were negative the second week and positive the third week.

TUBERCULIN TESTS ON CHILDREN. DR. ARTHUR H. STEELE, Northville, Mich.

This report is a brief summary of some work that has been done at the Wayne County Training School in conjunction with Dr. Henry Stuart Willis, of the Wm. H. Maybury Sanatorium at Northville, Mich. Tests were performed on 750 mentally deficient boys and girls, city born and city reared, white and Negro, from 9 to 16 years old.

The first study dealt with the reaction to two kinds of tuberculin after the first injection and after subsequent injections. Old tuberculin and Seibert's precipitated tuberculin were used.

Testing was done by intracutaneous injection; a small dose was followed two days later by a larger dose when the child failed to react and these two by a third and larger dose when the child still failed to react. The dilutions of old tuberculin used were 1:1,000, 1:100 and 1:10, and the amounts of precipitated tuberculin, 0.001 mg., 0.01 mg. and 0.1 mg. Dilutions were made on the day of the test; 0.1 cc. was injected into the skin of the forearm.

Thirty-three per cent of the 169 children tested with old tuberculin reacted to the 1:1,000 dilution. Subsequent tests, with larger doses, on the nonreactors brought the total percentage to 46.7. Only 25 per cent of the 421 children tested with precipitated tuberculin reacted to 0.001 mg., whereas the two subsequent tests on the nonreactors brought the total incidence of reactors to 73.8 per cent.

In the group retested with old tuberculin after one week there were 20 per cent more reactors; in that retested after one month, 25 per cent, and in that retested after three months, 20 per cent.

The retests on the 421 children tested originally with precipitated tuberculin showed an increase in reactors of 8 per cent at one week, 14 per cent at one month, 5 per cent at two months and 10 per cent at three months.

Many children received three doses of tuberculin in increasing amounts over a very short time, which may readily have excited an existing tuberculous focus. It has been contended by many persons that just this thing may happen. To anticipate it in part, 131 children not previously tested were given a single test and one week later were retested with the same dose. One group received old tuberculin and the other precipitated tuberculin; in both the incidence of the reaction to the retest was 11.4 per cent higher than that of the reaction to the original test, and the reaction to the retest was more intense in 16 per cent of the children.

To determine whether the newer, purified tuberculin products could be used by the Pirquet method, over 400 children were tested with crude old tuberculin, purified protein derivative, and precipitated tuberculin of varying strength. The dilution of the second and third products was made from tablets in some cases and from solution in others. When purified protein derivative or precipitated tuberculin in a concentration of 10 mg. per cubic centimeter was used, 12.4 per cent of the children reacted to the former and 13.3 per cent to the latter; 15.1 per cent reacted to old tuberculin. When a concentration lower than 10 mg. per cubic centimeter was used, there was a marked decline in the incidence of sensitivity.

INTRACUTANEOUS TUBERCULIN TESTS: A COMPARATIVE STUDY OF PURIFIED PROTEIN DERIVATIVE AND OLD TUBERCULIN IN SEVEN HUNDRED AND THIRTY-TWO INFANTS AND CHILDREN. DR. JOHN L. LAW, Ann Arbor, Mich.

This paper appears in this issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN, page 1220.

DISCUSSION ON PAPERS BY DR. STEELE AND DR. LAW

DR. HENRY STUART WILLIS, Northville, Mich: No pediatrician will accept the statement that from 85 to 90 per cent of children under 15 years of age will give a positive reaction to the tuberculin test. Such a high percentage of reactors would hardly be possible, because many efforts are being made to isolate carriers and get them into hospitals and thus decrease the incidence of tuberculosis. Twenty-five years ago the incidence of reactors to tuberculin was much higher than it is today. When tuberculin testing is applied day after day to children, the incidence becomes almost unbelievably high, too high to be accepted without serious question. The large number of children who react to the repetition of a dose that failed to produce a reaction before is surprising. When the child reacts the second time, it is suspected that he sustained some effect from the first test. Is one safe, then, in concluding that the patient has a tuberculous infection? Can an injection of tuberculin produce cutaneous sensitivity? I believe that reactions which develop after several injections are not true reactions to tuberculin.

I wonder if Dr. Law has seen a recent paper in the *American Review of Tuberculosis* in which the incidence of positive reactions was reported to be higher for old tuberculin than for purified protein derivative.

DR. PAUL KREITZ, Bethlehem, Pa.: I have fortunately been associated with the Henry Phipps Institute, where extensive work on tuberculin testing has been carried out. I should like to stress the incidence of reactors in different districts. In the high schools of Philadelphia about 92 per cent of reactors were found. In Minneapolis the percentage was much lower. The dilution of tuberculin must be fresh and standardized. Purified protein derivative is used entirely throughout the East. Tuberculin testing is more complicated than Schick or Dick testing. Aronson believes there is a definite relation between the intensity of the reaction to tuberculin and the clinical status.

DR. ROCKWELL M. KEMPTON, Saginaw, Mich: Dr. Kreitz remarked that the dilution must be fresh. May I ask how fresh?

DR. CLEMENT A. SMITH, Boston: Dr. Steele stated that in some of his cases the reaction had disappeared in forty-eight hours. I should like to ask his authority for calling that a positive reaction.

DR. ARTHUR H. STEELE, Northville, Mich.: Inflammation and induration, the two components of a reaction to tuberculin, were present. No one knows how long the reaction ought to last. I am sure that these reactions were more evanescent than the usual reaction, even with the first reactors in the series. Whether the reactors now under discussion are true reactors to tuberculin is a question to be determined. The evanescent character may indicate a nonspecific response.

DR. FRANK VAN SHOICK, Jackson, Mich: The percentage given by Dr. Steele seems quite alarming. Have the attendants in the institution been tested?

DR. ARTHUR H. STEELE, Northville, Mich.: The possibility that some one in the institution is spreading the disease has been carefully considered. In the ten years of existence of the institution only three persons with tuberculosis have been observed. One entered with tuberculosis, and one showed symptoms after having been there for some time. Our roentgenologist has been interested in the study of tuberculosis in children, and roentgenograms have been made of all persons in whom tuberculosis has been suspected.

DR. M. M. FENTON, Ann Arbor, Mich.: Any one doing considerable cutaneous testing has noticed differences in cutaneous reactions according to age. Allergic reactions are usually read from a few minutes to an hour after injection. Infants and small children, because of vasomotor instability, differ from adults in the cutaneous expression of their reaction to the injection of foreign protein. Can there be a parallel in delayed reactions to tuberculin?

DR. HENRY STUART WILLIS, Northville, Mich.: The reactions were usually present in twenty-four hours and had disappeared in forty-eight hours. They

persisted for at least a day. They differed from the ordinary allergic reaction, which lasts a much shorter time.

DR. ARTHUR H. STEELE, Northville, Mich.: The validity of these reactions has been questioned. I am not sure whether they should be called positive reactions to tuberculin. They were not present within the first eight or ten hours after injection. They were present at twenty-four hours and often disappeared in forty-eight hours. The story is presented as a study in progress rather than as a final report.

DR. JOHN L. LAW, Ann Arbor, Mich.: The main object in doing this study was to test the reliability and the potency of a new material. Stronger dilutions of old tuberculin in comparison with purified protein derivative could have been used and different results obtained, but the dilutions of old tuberculin were the ones commonly used in our clinic. There was no evidence that purified protein derivative sensititizes the patient to subsequent tuberculin tests. This recalls Dr. John Barnwell's work with small infants, in which as many as twenty injections of purified protein derivative did not sensitize to subsequent injections. The tuberculin test is an indicator which serves warning that tuberculous disease may be present, especially if there has been contact. Time and again, in subjects with a positive reaction to tuberculin for whom the roentgen findings are negative the disease develops in three, six or nine months without further contact and is demonstrable roentgenologically. In answer to Dr. Kempton's question, tuberculin is usually potent in a dilution of 1:1,000 for at least one week and in a dilution of 1:100 for two weeks, the material being refrigerated in both instances.

THE LEVINSON TEST IN THE DIAGNOSIS OF TUBERCULOUS MENINGITIS. JOHN ENGELFRIED, PH.D., Ann Arbor, Mich.

The Levinson test has been used for the past two years in our pediatrics laboratories as an aid in the diagnosis of tuberculous meningitis.

Tashiro and Levinson in 1917 published the results they obtained by using mercury bichloride and sulfosalicylic acid to precipitate spinal fluids. They used a 1 per cent solution of mercury bichloride as a metallic precipitant and a 3 per cent solution of sulfosalicylic acid as an alkaloidal precipitant. Their results show that normal spinal fluid gives a small precipitate with either of these reagents while the spinal fluid from a patient with meningitis gives a much heavier precipitate. The spinal fluid from a patient with tuberculous meningitis gives a much heavier precipitate with mercury bichloride than with sulfosalicylic acid.

At present a 2 per cent solution of mercury bichloride and a 5 per cent solution of sulfosalicylic acid are being used. One cubic centimeter of the spinal fluid is pipetted into each of two test tubes. To one tube is added 1 cc. of mercury bichloride and to the other 1 cc. of sulfosalicylic acid. These tubes are shaken, and 1 cc. of the contents of each is pipetted into a small agglutination tube having an inside diameter of 5 mm. The height of the precipitate in the tubes is measured at the end of twenty-four, forty-eight and seventy-two hours.

The spinal fluid from a patient with tuberculous meningitis generally gives a large precipitate with mercury bichloride, and the height of this precipitate is from four to six times the height of the precipitate obtained with sulfosalicylic acid.

The spinal fluids of 54 patients with meningitis were tested by the Levinson method. Of these, 16 fluids gave a positive reaction and 38 a negative reaction. Of the 16 patients whose fluids gave a positive reaction, 2 had received intraspinal injections of serum. Of the 14 remaining patients, 8 were proved clinically to have tuberculous meningitis, 1 to have Fott's disease with caseating miliary tubercles of the right lung, 1 to have residual poliomyelitis with tuberculosis of the right lung, 1 to have questionable influenzal or tuberculous meningitis (autopsy not performed) and 3 to have acute poliomyelitis.

The final diagnosis in 37 of the 38 cases in which the reaction to the Levinson test was negative was not tuberculous meningitis; however, in 1 case in which the

reaction was negative the condition was proved at autopsy to be tuberculous meningitis.

My impression of the Levinson test is that it is a valuable aid in deciding for or against a diagnosis of tuberculous meningitis. It is not pathognomonic.

DISCUSSION

DR. HAROLD B. ROTHBART, Ann Arbor, Mich.: I became interested in the Levinson test during my residency in Chicago and have had it carried out by Dr. Engelfried since my return to Ann Arbor. In certain cases of encephalitis or acute poliomyelitis the spinal fluid may or may not give a negative reaction. Dr. Engelfried cites 16 patients whose fluids gave positive reactions and states that only 8 of them had tuberculous meningitis but that others had tuberculosis in other parts of the body. I believe tuberculous meningitis has not been ruled out in the cases of the other 8 patients and that any spinal fluid with a low sugar content and a positive reaction to the Levinson test can with considerable accuracy be considered to indicate tuberculous meningitis unless this is definitely disproved.

DR. JOHN ENGELFRIED, Ann Arbor, Mich. Spinal fluid from a nontuberculous patient previously treated by intraspinal serum gives a positive reaction to the Levinson test because a change has been induced in the hydrogen ion concentration of the fluid. Had the test been applied at the time of the first tap, before the serum had been injected, the reaction would have been negative.

UNDESIRABLE REACTIONS TO TUBERCULIN. DR. HANS BEHRENDT, Frankfort, Germany (presented by DR. D. MURRAY COWIE).

The practice in Germany at the present time is to refrain from giving another dose of tuberculin if the reaction to a preceding one has been positive, because not infrequently an unpleasant or perhaps a serious reaction occurs. Fourteen illustrations are recorded, the two cases reported hereafter being examples.

In a girl 4 years old, the fifth healthy child among 6 tuberculous brothers and sisters, pain suddenly developed in the right knee, and she became unable to walk. The reaction to the Moro tuberculin test was found to be positive. Roentgen examination showed early tuberculosis of the knee joint. A plaster dressing was applied and kept on for two months; it was then removed and replaced by a lattice splint, which enabled the child to go to kindergarten. At this school it was the practice to perform tuberculin tests on all the children. A Moro test was done by the nurse in charge. The following day there was severe swelling of the knee, making it necessary for the dressing to be opened. After two days the swelling had not subsided, and the child had to be hospitalized. It was two weeks before she could be discharged. Unpleasant complaints by the parents followed. This is a typical case of an undesirable focal reaction to tuberculin—the tuberculous focus grew worse. This goes to show that when serial or routine tuberculin tests are being carried out children who have previously had a positive reaction to tuberculin and those who are strongly suspected of having active tuberculosis should not be tested.

A boy of 15 had had glandular swelling of the neck since early childhood; this swelling had become more pronounced in recent years, with submaxillary and axillary enlargements the size of a hen's egg. The reaction to the first Moro tuberculin test, done in 1911, was positive. The caseous glands were excised. In 1912 a Pirquet test was done at the same time as an intradermal tuberculin test with 0.5 mg. of old tuberculin. After twenty-four hours marked fever, vomiting and profuse diarrhea developed. The next day the color of the face changed, and the throat, eyelids, nose and lips swelled enormously. A spotty exanthem was present on the body, and the sensorium was greatly affected. The third day the tip of the nose became blue-black. The site of the Pirquet test healed without a reaction. The area of the reaction to the intracutaneous test was the size of a silver dollar and was covered with purpuric spots. The right knee was blue-green. The fourth right toe and the third left toe were gangrenous. The fever declined and the

gangrenous areas sloughed off in the course of a few days. Healing occurred with loss of tissue.

This is a severe toxic-allergic reaction in a sensitized child. As tuberculous allergy had been proved, the intracutaneous and the Pirquet test were not necessary. Under no circumstances was it permissible to ignore the first reaction and to start with such a strong dose of tuberculin injected intracutaneously. The injuries produced could have been avoided.

DISCUSSION

Dr. Thomas B. Cooley and Dr. D. Murray Cowie called attention to the rarity of such reactions in their hospital experience, to the general custom in America of using not more than 0.1 mg. of tuberculin for the first test dose and to the custom when there is a history of tuberculosis in the family of using 0.01 mg. for the first test dose.

INFECTIONS OF THE THROAT IN TUBERCULOUS CHILDREN. DR. GERTRUDE MITCHELL, Northville, Mich.

An epidemic of sore throat in tuberculous children is reported, in which most of the patients had the childhood type of tuberculosis. Of 121 children, 89, or 73.5 per cent, were affected. Many had more than one attack. The cultures of material from the throat did not show streptococci or hemolytic streptococci in some cases. These cases are included in the report because of the typical clinical picture and course of the disease. A sudden high fever accompanied by sore throat and headache and sometimes by abdominal pain was the usual picture. The throat was extremely red, and the tonsils were red and swollen and frequently covered with grayish yellow patches of membrane. The tongue often resembled that of a patient with scarlet fever. The cervical glands were enlarged and tender. The nasal discharge was slight. The tympanic membranes of the smaller children at the height of the epidemic were frequently exceedingly red, the redness often extending a short distance down the external canal. The fever subsided in from one to five days, and all the symptoms disappeared one or two days later. Boys and girls were equally affected. The children under 4 years of age had severer infections and more frequent and disturbing complications than the older ones. The incidence was no higher than in similar epidemics among other children, but infections of the ear and pulmonary complications were more frequent. Twenty-seven per cent of the children had otitis media (15.5 per cent, suppurative). Pneumonia occurred in 5.6 per cent and bronchitis in 4.4 per cent. More children showed roentgen evidence of an increase in the extent of their tuberculous infection than usually do in routine check-ups of an equal number of children. Fourteen showed such an increase. Of 12 children who were ill during this period and were not considered in the report, 4 also showed an increase. The total number showing an increase in the extent of their infection was 18, or 14.8 per cent of all the children in the hospital; 5.6 per cent of a group of 106 children had shown an increase during the same period the previous year.

The results of the Dick tests did not vary greatly from those reported in similar epidemics among nontuberculous patients.

There was a tendency for reinfections to occur; 20 children had two attacks, and 4 had three; 1 showed rheumatic symptoms six weeks after the acute infection of the throat, and 2 had heart murmurs suggestive of mitral involvement. Little information is available in the literature regarding simultaneous tuberculous and streptococcic infections. Our findings here do not agree with those of Antoniazzi, who concluded that tuberculous lesions, particularly those of the lungs, do not show definite change (qualitative or quantitative) during a streptococcic focal infection.

DISCUSSION

DR. CLEMENT A. SMITH, Boston: I want to congratulate Dr. Mitchell and to say that this question of cultures of material from the throat showing hemolytic streptococci has been investigated by physicians in Boston. They made a survey

of a nursery of new-born infants, culturing material from the throats of normal babies under 2 weeks of age. About half of them had cultures positive for the hemolytic streptococcus.

Dr. Gertrude Mitchell, Northville, Mich.: We did find in some cases that no streptococci were reported in cultures taken on the first day of the infection but that a few days later Streptococcus viridans or Streptococcus haemolyticus was observed.

Prolonged Bleeding Time in Acute Pyelonephritis. Dr. Rockwell M. Kempton, Saginaw, Mich.

An infant 12 weeks old born at the eighth month of a mother suffering from marked nephritic toxemia, whose weight at birth was 3 pounds and 10 ounces (1,590 Gm.), was hospitalized for premature care until he was 6 weeks old. Soon after he was taken home, nasopharyngitis developed, with fever (from 100 to 104 F.), irritability and anorexia. Pyuria, with much albumin and many colon bacilli (proved by culture), was found. The urine soon became bloody, and a diagnosis of acute hemorrhagic nephritis was made. A bulging ear on the right and a lesser degree of involvement on the left were found. Double paracentesis was done. The right ear started to bleed, and a free hemorrhage continued for thirty-six hours. The left ear started bleeding a few hours after the right, and so did the site of each transfusion. At the time of the second transfusion the child's condition seemed hopeless. Blood transfusions, the administration of calcium gluconate and coagulin and the local application of hydrogen peroxide and epinephrine had little effect in checking the hemorrhage. After the intramuscular injection of 10 cc. of diphtheria antitoxin (for the effect of the horse serum) the hemorrhage was controlled. It is interesting that the coagulation time on the second and the tenth day in the hospital was found to be within normal limits. There was no evidence of purpura. The free bleeding must therefore have been due to a prolongation of the bleeding time incident to the systemic infection.

Summary.—The case presented is one of pyelonephritis with complicating otitis media in a premature infant. The urine became hemorrhagic and after double paracentesis and three blood transfusions hemorrhages took place from every point incised. No check in the bleeding was secured until after 10 cc. of horse serum was injected. The improvement after the use of horse serum (antitoxin) seemed definite. The transfusions were a life-saving measure. The point is stressed that pediatricians practicing apart from medical centers should take the responsibility of training some one in their community to become expert in the art of giving transfusions to infants and children, to handle emergency conditions in which the loss of blood is a factor and to give their juvenile patients who are in need of supportive treatment in the form of blood transfusions the same consideration given adults. The members of the medical profession in general must be taught that babies can be given transfusions.

DISCUSSION

Dr. Mark Osterlin, Traverse City, Mich.: I should like to stress the importance of pediatricians familiarizing themselves with the technic of blood transfusions and intravenoclysis. I was recently in a well equipped hospital in which a baby had never been given a transfusion. Practitioners in rural communities are fearful of giving transfusions. There should be some one close at hand in each community capable of carrying out these life-saving measures.

Dr. Harold B. Rothbart, Ann. Arbor, Mich: For the purpose of checking the bleeding would it be more effectual to give the blood intramuscularly than intravenously? The tissue response seems different. Would it have been better to have given the blood intramuscularly?

Dr. Rockwell M. Kempton, Saginaw, Mich.: I do not think so. The indications called for a form of treatment which would replace the blood lost and also

supply the element or elements needed to bring about normal clotting. While intramuscular transfusion is often a great convenience as a method of getting antibodies and certain elements of the blood into the system, I do not believe it would have been applicable here. The quantity of blood administered would necessarily have been much smaller, and the elements concerned with coagulation might as well enter the system through the blood stream as by absorption from the muscles. Failure of the blood to clot after the second transfusion had brought it up to the normal level tended to show that to bring about a restoration of normal clotting it was necessary to do something more than merely replace the blood lost. In this instance the horse serum of diphtheria antitoxin seemed to do the work. There is on the market a precipitate of horse serum (called coagulose), but it is rather expensive. It may be well to remember that if necessary some other form of horse serum may be used and that diphtheria antitoxin may well serve the purpose.

TREATMENT OF ACID-BASE DISTURBANCES. DR. GEORGE M. FRAUENBERGER, Cincinnati.

The exact nature of the acid-base disturbance can be told only by quantitative studies; the most practical method is the determination of the carbon dioxide content of the blood serum. When this is known, one need not be afraid to inject slowly a calculated amount of acid or base intravenously.

Correction of the acid-base disturbance is not the whole story in therapy, although it plays the major rôle. One should use other measures—restore normal buffer values, promote renal activity, aid respiration and relieve the primary cause. To calculate the dose of bicarbonate the following formula is used: grams of sodium bicarbonate = (55 volumes per cent—determined carbon dioxide content) $\times$ 0.026 $\times$ weight in kilograms. A simple proportion converts the dose in grams to cubic centimeters of 4 per cent solution of sodium bicarbonate. Bicarbonate is given intravenously only when the carbon dioxide content is below 40 volumes per cent.

For convenience, a similar acid formula is used. The acid must be properly diluted and given only in calculated amounts by one skilled in its use.

In cases of severe involvement equal amounts of physiologic solution of sodium chloride or Ringer's or lactate-Ringer (Hartmann's) solution and 5 per cent dextrose are administered subcutaneously or intravenously. After the initial single injection continuous intravenous drip is started, and it is continued five or six days or less if the response is good. Not more than 90 cc. of fluid per pound (453 Gm.) of body weight per day is given to babies. To children 6 years old not more than 2,000 cc. and to older children not more than 3,000 cc. is given daily. If edema occurs, it is not necessary to stop the drip. The rate is diminished to 10 or 12 drops a minute and the solution changed to 10 per cent dextrose; 5 cc. of calcium gluconate is given intramuscularly before the administration of bicarbonate or blood transfusion by the indirect citrate method. To infants, 10 cc. of blood per pound (453 Gm.) of body weight is given per day. Renal activity is stimulated by fluids administered intravenously. If necessary, respiration is stimulated by the hypodermic injection of caffeine with sodium benzoate or some other stimulant.

The acid-base balance in persons in diabetic coma is cared for by the administration of insulin and fluids. It is sometimes advisable to correct severe acidosis speedily with sodium bicarbonate.

From Jan. 1, 1935, to Oct. 1, 1936, 276 patients were admitted to the Cincinnati Children's Hospital with gastro-enteritis. Of this series 49 acquired acidosis, with a carbon dioxide content lower than 30 volumes per cent, and 23 died; 9 patients were moribund on admission, and 9 had associated complications—bronchopneumonia, sepsis or congenital syphilis—or were premature. Two patients with salicylate acidosis and one with nondiabetic ketosis recovered.

Of the 5 patients with alkalosis whose carbon dioxide content was over 85 volumes per cent, only 1 recovered. It seems to be much harder to treat patients with alkalosis. Physicians and laymen must be taught not to give large doses

of the apparently harmless "soda." Sixty per cent of the 56 patients with acidosis were successfully treated with alkali.

DR. WILMA SACKS, Ann Arbor, Mich.: Have you ever seen a patient with alkalosis whose only symptom was vomiting?

DR. GEORGE M. FRAUENBERGER, Cincinnati: Yes, one sees such patients. Unless the carbon dioxide content is above 90 volumes per cent, fluids administered intravenously will suffice.

DR. HAROLD B. ROTHBART, Ann Arbor, Mich.: I am surprised that Dr. Frauenberger does not say something about sodium lactate. The use of sodium lactate is not dangerous. The dose suggested is 60 cc. of a sixth-molar solution. This solution can be given either intravenously or subcutaneously, and within a period of from two to three hours the carbon dioxide content may be adequately raised. Furthermore, I should like to question the diagnosis of alkalosis. I wonder if the hyperpnea was not a condition of acidosis rather than of alkalosis.

DR. GEORGE M. FRAUENBERGER, Cincinnati: As far as the use of sodium lactate, as advocated by Dr. Hartmann, of St. Louis, is concerned, the main object in giving this paper was to bring the experiences of the physicians at the Children's Hospital to this group and to show other points of view. I feel that usually it does not make much difference whether one uses sodium lactate or sodium bicarbonate, provided a quantitative estimation of the carbon dioxide content is obtained and a calculated amount is given. Sodium bicarbonate seems to be more efficient when the carbon dioxide content is low. It must be stressed that only calculated amounts of sodium bicarbonate should be given. Regarding Dr. Rothbart's second question, the diagnosis of alkalosis or acidosis can definitely be made only by determining the carbon dioxide content of the blood. Clinically, hyperpnea is usually seen when the carbon dioxide content is low, but I have even seen rapid, shallow breathing in cases of alkalosis. It is easy to be fooled if quantitative studies are not obtained.

ANALYTIC REPORT OF FOUR CASES OF LEAD POISONING. DR. ROBERT MCGILLICUDDY, Lansing, Mich.

Four unrelated children were seen in the Cincinnati General Hospital in a two and one-half month period beginning July 1, 1935. Three were boys and 1 a girl, all were approximately 2 years old, and 2 were white and 2 Negro. All had essentially unimportant histories. In no instance could the source of the lead poisoning be definitely proved. Two of the children were admitted in convulsions and 2 with symptoms referable to the gastro-intestinal tract—vomiting, constipation and diarrhea. Only 1 had abdominal pain as a symptom. The temperature of each was normal on admission and became elevated later in the course of the disease. Studies of the blood of each showed stippling, but none had anemia. Spectroscopic determination of the amount of lead in the urine, blood and spinal fluid showed uniformly high levels; in a few instances the content was appreciably increased when the child returned to a normal diet from a diet high in calcium.

The spinal fluid of the 4 patients showed definite evidence of meningeal irritation and an increase in the globulin content and in the number of cells. The blood and the spinal fluid showed increased values for sugar. Roentgen evidence of the lead line was present in all cases. Three children recovered with apparently no ill effects; 1 died, and the lead content of the tissues was found to be exceedingly high.

DISCUSSION

DR. CLEMENT A. SMITH, Boston: A number of similar cases have been observed the past few years in Boston. They are distressing. I should like to ask some one from Detroit how many occur there.

DR. SAMUEL LEVIN, Detroit: I shall ask Dr. Cooley to answer that question, as he observes most of these cases in Detroit.

DR. THOMAS B. COOLEY, Detroit: Nearly all our cases have been in females among the poorer people who burn old batteries in their stoves. This has been

the recognized source of the poisoning in most of our cases. There were several cases in Negroes in the neighborhood of our hospital, in most of which the poisoning was due to inhalation of fumes from burning batteries.

DR. HARRY TOWSLEY, Ann Arbor, Mich.: I should like to ask Dr. Smith if the lead poisoning in Boston could be traced to old lead plumbing pipes.

DR. CLEMENT A. SMITH, Boston: Old lead plumbing pipes are no longer considered to be a frequent or potent factor in the production of lead poisoning. Cases have occurred in babies owing to the mother's wearing a lead nipple shield. In one case roentgen examination of the abdomen of an infant, showing the lead line in the bones, revealed flecks of paint in the stomach.

DR. ROBERT MCGILLICUDDY, Lansing, Mich.: The interesting thing was that there was no reason to suspect lead poisoning until the taking of a roentgenogram in the first case, for other reasons, showed the lead line and made the staff lead conscious thereafter.

OPEN FORUM

IN CHARGE OF DR. THOMAS B. COOLEY

THE SPLEEN AND SOME TYPES OF ANEMIA. DR. THOMAS B. COOLEY, Detroit.

THE FUNCTIONS OF THE SPLEEN

Of the many functions, normal and pathologic, which have been, on evidence of varying validity, attributed to the spleen, the following are of importance to the present subject.

1. *The Reservoir Function.*—This is well established and seems normally to play an important part in regulating the blood flow to meet varying demands. In certain pathologic states to be considered, a perversion of this function underlies certain serious, sometimes fatal manifestations of the disease process.

2. *Formation of Blood.*—During intra-uterine life, the production of all types of blood cells is normal to the spleen, as to other parts of the histiocytic system. After birth, the myeloid activity subsides rapidly, though it can be readily revived in pathologic states. The production of lymphocytes and phagocytes, as would be expected from the organ's structure, apparently continues throughout life.

3. *Destruction of Blood.*—There is no question as to the important rôle that the spleen, as part of the histiocytic system, plays normally in the results of the disintegration of red cells. Its peculiar structure fits it particularly to be the "graveyard" of worn-out cells. The production of bilirubin is a part of this process.

The spleen's part in pathologic hemolysis is a different matter. The effect of splenectomy in cases of hemolytic icterus and recently in a few cases of erythroblastosis of the new-born leaves no doubt that splenic action is important in the pathogenesis of these diseases, but the precise nature of the action is not clear. Though the cells tend to return to normal shape and resistance after splenectomy, this does not prove that the spleen is more than indirectly responsible for the abnormalities or that the actual destruction is performed by the spleen. The precise nature of the process is not known.

Phagocytosis of whole erythrocytes in the splenic maze may be observed and seems to be important in sickle cell anemia. I have not found it striking in other types of anemia. There is no evidence that the spleen has any part in the most common type of destruction, that by fragmentation, except in the disposal of the fragments.

4. *Hormonal Action on the Bone Marrow.*—Contradictory theories are advanced as to the influence of the spleen on the marrow function. One authority assumes a stimulating action; another recommends splenectomy in cases of hypoplastic states to remove a depressant factor; still another postulates a regulating action which may be either stimulant or depressant. Possibly one might assume a normal stimulant and a pathologic depressant function.

SPLENIC ACTION IN DISEASE

Erythroblastosis of the New-Born.—No definite knowledge of the etiology and the pathogenesis of this highly fatal hereditary disease exists. The spleen is enlarged and displays marked myeloid activity. Extreme hemolysis, apparently neither by fragmentation nor by phagocytosis, is part of the picture, and it is a fair hypothesis that the process may be a type of "hypersplenism" similar to that of hemolytic icterus. Cessation of the hemolysis after splenectomy supports this idea.

Hemolytic Icterus.—The peculiarities in the form of the red cells in this disorder and their susceptibility to hypotonic solutions are well known. Recent studies seem to indicate chemical abnormalities in the structure of the cells. Excessive hemolysis is either constant or intermittent, and it apparently occurs neither by fragmentation nor by phagocytosis but by an unexplained process in the mazes of the spleen and somehow related to the decrease in resistance. The almost invariable effect of splenectomy, both on the hemolysis and on the form and the resistance of the cells, is evidence of the spleen's importance in the pathogenesis, though its action has not been explained.

The hemolytic crises, or "crises of deglobulization," in this disease and in sickle cell anemia illustrate a striking perversion of the reservoir function of the spleen. Though these crises are spoken of as hemolytic, there may be no evidence of increased hemolysis. The essential thing is a tremendous dilatation of the spleen due to the withdrawal of erythrocytes, which occasionally results in death and which, though there is no bleeding vessel, has the characteristics of fatal hemorrhage.

The occasional failure of splenectomy in cases of this disorder, particularly of the acquired form, may be due to the growth of supernumerary spleens or to the taking over of the splenic function by other depots of histiocytic tissue.

Sickle Cell Anemia.—The strong hereditary character, the peculiar cell forms and the splenic crises suggest a close relation between this disease and hemolytic icterus. The spleen's part in the pathogenesis is not so evident here, however. Hemolysis is by phagocytosis and fragmentation and is little affected by splenectomy. Thrombosis in various sites is a common feature and seems to be the main reason for the progressive splenic atrophy. Splenectomy in early childhood appears to have some beneficial effect on anemia and on the episodes of pain in the abdomen and extremities which are probably due to thrombosis. Apparently there is a more general involvement of the histiocytic tissues in sickle cell anemia than in hemolytic icterus, so that removal of the spleen brings about relatively slight improvement.

Erythroblastic (Mediterranean) Anemia.—In spite of the great enlargement of the organ, there is even less evidence of any primary splenic activity. The cell picture is bizarre, both physically and chemically, and is little changed by splenectomy, except for a curious increase in the number of normoblasts. Hemolysis, chiefly by fragmentation, is not definitely affected by the operation. The disease cannot be looked on as primarily or chiefly a splenic disorder.

Essential Thrombocytopenic Purpura.—From striking analogies between this disease and hemolytic icterus, both in the clinical course and in the effects of splenectomy, it is natural to assume that the spleen acts on the platelets in the former as on the red cells in the latter. This is not proved, however, and in the secondary, often transient type there seems rather to be hypoplasia of the platelet-forming tissue. While splenectomy is almost as successful in cases of thrombocytopenic purpura as in cases of hemolytic icterus, care should be taken to differentiate the idiopathic from the secondary form, as patients with the latter often recover without operation and when they do not the failure may be due to true platelet aplasia.

Splenic Anemia and Related Disorders.—The present tendency in pediatric literature is to limit the term splenic anemia to the first stage of the Banti syndrome, which is essentially progressive cirrhosis of the liver and the spleen. A number of other conditions present a similar combination of splenomegaly,

leukopenia and somewhat increased breakdown of cells, but they do not progress in the manner of Banti's syndrome, and criteria for distinguishing those which will go on to hemorrhage and cirrhosis are not clear. It is therefore not easy to evaluate claims for the benefit of early splenectomy. It is probable that in some cases the cirrhotic process is arrested by the operation, though it is hard to assign a reason. If one is convinced of the value of the operation in cases of splenic anemia, it might be considered indicated by most of the obscure splenomegalies of childhood.

In cases of the apparently related condition characterized by early bleeding from esophageal or gastric varices, splenectomy seems to have scored more definite successes.

DISCUSSION

Dr. Henry G. Poncher, Chicago: Dr. Cooley has succinctly characterized the clinical and the scientific knowledge of the splenic factors in the various types of anemia of infancy and childhood. It is apparent from his appraisal that little information exists as to whether the splenic alteration is the primary, or initiating, factor. Since, as Klemperer pointed out, the spleen may be involved in many fundamentally different morbid states, one always has to entertain the possibility that the splenic disturbance may be secondary. Information on the structure and the function is meager, probably for the reason McNee gives, that the spleen has no function absolutely essential to life and some more indirect reason for its presence in the body has to be discovered. No striking clinical phenomena are seen after splenectomy that are in any way comparable to those seen after thyroidectomy or the extirpation of other organs. It seems prudent, therefore, not to endow the spleen with any function it does not possess. The first two splenic functions enumerated by Dr. Cooley are well established by clinical and experimental evidence. The part played by the spleen in the destruction of blood and the activity of the bone marrow is less clearly defined, as he has indicated.

Regarding the splenic action in disease, little more is known. In the case of erythroblastosis of the new-born, it is difficult to see why the cessation of hemolysis after splenectomy supports the hypothesis of "hypersplenism." It would be difficult to explain the beneficial effects of repeated blood transfusions without splenectomy on the same hypothesis. It seems rational to regard the condition, as Klemperer has done on the basis of histiologic study, "as a result of arrested development caused by an alteration in the coordinate development of the various centers of the hematopoietic mesenchyme." The familial incidence which may be demonstrated in many of the cases would be in harmony with such a concept. With essential thrombocytopenic purpura, despite the unquestionable success of splenectomy in properly selected cases, the microscopic study of the extirpated spleen does not disclose any characteristic morphologic alteration which would account for the supposed thrombocytolytic function. Clinical evidence is likewise not in keeping with such a hypothesis. Likewise, there is lack of correlation between the success of splenectomy and the histologic evidence for a primary blood-destroying factor of the spleen in hemolytic icterus.

Out of this chaos of conflicting observations should come the realization and the frank admission that one cannot invoke explanations of the rôle of the spleen in anemia on the basis of present thinking. Dr. Cooley has exemplified this in his talk. While more facts would permit a more enlightening concept, the critical use of those available would prevent much of the confusion that now exists.

Dr. S. M. Goldhammer, Ann Arbor, Mich.: Although Dr. Cooley has adequately reviewed the current views regarding the functions of the spleen, one has the impression that theory rather than fact still has the upper hand in this problem. It is peculiar that the spleen is enlarged by two different, distinct processes: overproduction and destruction of the red blood cells (polycythaemia vera and hemolytic jaundice). Further, in sickle cell anemia, which appears to be a hemolytic disease and similar in many respects to acholuric jaundice, the spleen is atrophied. In cases of hemolytic jaundice, splenectomy is of material benefit to the patient, but the red blood cells remain spheroid and small, and their fragility does not always

return to normal. Removal of the spleen in cases of polycythaemia vera and sickle cell anemia is of no benefit.

Another interesting form of splenomegaly, so-called Banti's disease, contrary to the usual teaching, is not materially aided by removal of the spleen. The very existence of this disease can be questioned. Since Banti's original description, experimental and clinical evidence has accumulated sufficient to show that it is not a clinical entity and cannot be differentiated pathologically from other forms of splenomegaly associated with congestion. In a series of 41 cases of so-called Banti's disease, in 24 of which splenectomy was performed and in 17 of which there was no operation but the patient was treated symptomatically, there appeared to be little question but that the prognosis was much better if the operation was omitted.

Dr. Clement A. Smith, Boston: My co-workers and I have given up taking out the spleen for thrombocytopenic purpura because we feel that the patient is not uniformly improved after splenectomy and because we have found an increase in the number of patients whose purpura gradually disappeared after diet, vitamin and transfusion therapy. I should like to ask Dr. Cooley if he is having fewer patients wtih thrombocytopenic purpura splenectomized.

Dr. Thomas B. Cooley, Detroit: I try to select my patients very carefully; about three of four are not operated on. I usually tell the parents to bring the child back in case of a recurrence. Most of the children never have a second attack. If a child has had prolonged or recurrent thrombocytopenic purpura and the condition cannot be managed in any other way it is advisable to operate. I wish that Doctor Goldhammer would tell me something about the cases in which biopsies of the bone marrow were done. Some authorities do not believe that the platelets are manufactured by the bone marrow.

Dr. S. M. Goldhammer, Ann Arbor, Mich.: Concerning the 41 cases of hepatolienal cirrhosis previously mentioned, splenectomy was performed in 24. The operative mortality was 30 per cent. Of the remaining 17 patients, studied for a period of at least 10 years, 7 died, 5 were improved and 5 were not improved. In a comparative group of 13 cases in which an operation was not performed, 5 patients are dead, 6 were improved and 2 were not improved. It is my opinion that Banti's disease per se does not exist and that splenectomy in many instances is performed on persons with cirrhosis of the liver. The anemia in hepatolienal cirrhosis may result from hemorrhage, the failure of storage of the "active" principle for normal hematopoiesis or a combination of the two factors. There is no specific treatment for cirrhosis, but if the anemia is eliminated and the patients are given a diet high in carbohydrate, they will live as long or longer than patients who have had a splenectomy. This treatment is not a cure but is palliative.

Splenectomy in cases of thrombocytopenic purpura, although usually associated with remarkable improvement, may be of no benefit. If the spleen is overactive and destroys the platelets in excessive numbers, its removal is indicated; however, if the decrease in the number of thrombocytes is the result of a disturbance in the production in the bone marrow, splenectomy is of little value. One may gain some insight as to which mechanism is involved by studying the bone marrow before operation.

Dr. Harold B. Rothbart, Detroit: If there is such a thing as Banti's disease, why is it that the spleen is so much larger than the liver? I assume we are dealing with cirrhosis of the liver.

Dr. S. M. Goldhammer, Ann Arbor, Mich.: Cirrhosis of the liver is not necessarily associated with splenomegaly. The latter is dependent on the pathologic changes in the walls of the blood vessels and the size of the lumens of the blood vessels. The greater the obstruction in the portal system, the more the congestion and stasis behind the obstruction.

Dr. Thomas B. Cooley, Detroit: I have never made a diagnosis of Banti's disease. I think the diagnosis that fits the condition best is splenic thrombophlebitis. There are still a number of problems on which light will gradually be thrown. A little more is known about the effects of splenectomy than was formerly known.

TUMOR OF THE BRAIN IN CHILDREN. DR. LOUIS M. HARLEY, Ann. Arbor, Mich.

The cases of tumor of the brain in children observed in the University Hospital since 1925 were reviewed. It was found that the disease may simulate various conditions, including chorea, so-called cyclic vomiting, epilepsy, poliomyelitis, spastic hemiplegia, error of refraction, meningitis and appendicitis. The patient may be treated for months, in fact years, for these diseases before a correct diagnosis is made. By that time atrophy of the optic nerve is so far advanced that even though complete eradication of the tumor can be accomplished, nothing can be done for the return of sight. Use of the ophthalmoscope earlier in the course of the illness might have prevented such an outcome.

Generalized symptoms of intracranial pressure usually appear early but may appear later in a child than in an adult because of the separation of the sutures and the progressive enlargement of the head.

Vomiting and headache are the most common symptoms; one may occur without the other. Vomiting usually appears early in cases of subtentorial lesions. Projectile vomiting occurs infrequently and is not to be expected; when present it is more in favor of an intracranial lesion, especially when it appears unaccompanied by nausea when the child awakes in the morning. Fundoscopic examination should be done in all cases of continued or intermittent vomiting.

The site of the headache usually helps little in the localization of the lesion. The headache may be mild and of short duration or continuous and severe. It is frequently described as "lifting the top of the head off." An abnormally slow pulse rate is uncommon in cases of tumor of the brain. It is more frequently an indication of the acute increase in pressure found in association with abscess of the brain or injury to the skull.

Incoordination of movement is an important finding in cases of subtentorial lesion or cerebral tumor. Locomotor or intention ataxia especially limited to one upper extremity indicates a lesion in the cerebellar hemisphere on that side. Astrocytoma is more common in this region. A midline lesion is usually a medulloblastoma, which induces a static type of ataxia—incoordination on standing, with a wide base and definite asynergia of the trunk. The gait is staggering, or drunken. Usually the four extremities are involved.

Strabismus and diplopia are not uncommon in cases of cerebellar neoplasm in children. The history of impairment of the vision cannot be depended on. Marked papilledema and atrophy of the optic nerve may exist without a complaint. Normal fundi may be found in cases of tumor of the brain. Papilledema usually occurs late in cases of lesion of the posterior fossa. Homonymous hemianopia localizes the lesion at the base of the brain, on the contralateral side, anywhere in the visual system from the optic chiasm to the occipital lobe.

Facial paralysis, commonly of the peripheral type, occasionally accompanies cerebellar tumor, especially tumor of the pontile angle involving the sixth, seventh or eighth cranial nerve.

Severe abdominal pain simulating appendicitis may occur. This is a referred pain, an expression of irritation of the vagus nuclei.

Stiffness of the neck and definite meningeal signs may accompany tumor of the posterior fossa, especially when the tumor grows toward the foramen magnum. If meningitis is suspected, a fundoscopic examination should precede spinal puncture. Removal of fluid in cases of tumor of the posterior fossa may cause sudden release of pressure, herniation of the cerebellar tonsils into the foramen magnum, compression of the medulla and sudden death.

In the University Hospital, spinal punctures are not done and encephalograms are not made if there is any choking of the disks or if tumor of the posterior fossa is suspected; instead, ventriculographic studies are done if the lesion cannot be localized otherwise. They almost invariably demonstrate a tumor if one is present, and they localize it in 97 per cent of the cases.

There are cases of tumor of the brain in which neurologic examination, examination of the fundi and roentgen examination of the skull reveal nothing abnormal. The history may be strongly suggestive. Frequent periodic fundoscopic examinations should be done.

DISCUSSION

Dr. C. F. List, Ann Arbor, Mich.: I should like to make a few remarks from the neurologic standpoint. In all cases of suspected tumor of the brain, particularly when choked disks are present, a lumbar puncture should be avoided or, if done, should be performed with the utmost care. Recently I observed a comatose child with marked meningeal signs whose disks were beginning to be choked. A ventricular puncture was performed, and the condition was found to be tuberculous meningitis. If it had been tumor of the brain, the child's life might have been saved by the decompressive puncture, but because it was meningitis, the diagnosis could be made as well from the ventricular fluid.

Many authorities believe that the outlook for children with tumor of the brain is hopeless. As a matter of fact, the outlook is excellent with certain types of tumor if the diagnosis is made early (astrocytoma of the cerebellum, for instance). It is true that a tumor involving the brain stem has a hopeless prognosis. In the University Hospital it is believed that every tumor of the posterior fossa should be verified by operation before roentgen ray treatment is given. This seems justified because in certain cases in which the clinical picture is that of tumor of the posterior fossa, the condition may turn out to be inflammatory (arachnoiditis). Roentgen therapy without preceding decompression may lead to a severe roentgen reaction or even to death. In cases of cerebellar-medullar blastoma the main portion of the tumor should be removed by the operation in order that the circulation of the cerebrospinal fluid may be restored. Then roentgen treatment is given not only over the operative site but over the entire central nervous system, to prevent metastasis due to implantation.

Dr. Vincent C. Johnson, Ann Arbor, Mich.: Roentgenology plays an important part in localization of all tumors of the brain in patients of all ages. Routine roentgen examination of the skull is of localizing value only in a small percentage of cases: when the site of the tumor is revealed by localized proliferative or destructive changes or when an abnormal intracranial calcium deposit is demonstrable. Since the routine examination of the skull usually reveals only the generalized changes produced by increased intracranial pressure, it is necessary to employ a more difficult procedure, encephalography or ventriculography, to localize the majority of the lesions. Ventriculography is usually preferable. Encephalography is not used in the University Hospital when the intracranial pressure is markedly elevated. Pneumographic localization has been found to be accurate, and it is now possible to demonstrate preoperatively the exact site of practically all tumors of the brain.

Dr. C. F. List, Ann Arbor, Mich.: It is not safe to make an encephalogram in cases of suspected cerebellar tumor. If choking of the disks or separation of the suture lines is present, a ventriculogram is preferable.

Dr. Louis M. Harley, Ann Arbor, Mich.: Medulloblastoma is the only tumor of the brain that metastasizes to the spinal cord. This metastasis appears to be the result of interference, as it does not occur unless removal of material for biopsy or removal of the tumor is attempted. Nevertheless, decompression should be done and tissue should be removed and examined before roentgen therapy is begun; otherwise, if a supposed medulloblastoma proves to be an astrocytoma, which is not amenable to irradiation, atrophy of the optic nerve will develop and permanent blindness may result.

Variability of the Kahn Reaction in Children.

Dr. Harold B. Rothbart, Ann Arbor, Mich.

The specificity of serologic tests for syphilis is not indisputable, and such tests should be regarded in the same light as other laboratory procedures when one is making a clinical diagnosis.

This report concerns 12 apparently nonsyphilitic children seen in the past two years in the University Hospital whose Kahn reactions of the blood were positive on one or more occasions. They represent approximately 0.18 per cent of the

new patients seen in the pediatric clinic during the same period. The incidence of the false positive reactions is small, but the rarity of such reactions does not minimize their importance. Infection, acute or chronic, was present in all except 1 case. Infection therefore appears to be an important cause for the false serologic reaction. Technical errors cannot be entirely overlooked but seem unlikely in view of the highly trained personnel under the direction of Dr. Kahn. Other serodiagnostic tests for syphilis may not have given false results, but this is improbable in view of the low incidence of false serologic reactions obtained with the Kahn (standard) test as compared with the incidence of those obtained by other methods. There was no definite relation between the temperature of the child and the positive reaction. In all instances except 1 the reaction finally became negative. In this case the Kahn reaction was only 1 plus. The test was not repeated; the child was normal, and there was no history of syphilitic infection in the family.

It is essential to recognize that a positive serologic reaction does not always indicate syphilis. My plea is against a hasty diagnosis of syphilis based on a positive reaction with no other evidence to support the diagnosis. If there are no clinical manifestations of syphilis and the family history contains no evidence of syphilis, repeated serologic tests should be made. In my opinion false positive reactions may persist for several weeks or longer, and the tests should be repeated at frequent intervals before antisyphilitic therapy is instituted. Once treatment is begun, it may be difficult to determine the child's status accurately should the serologic reaction subsequently become negative.

Infants and children suffering from acute or chronic infection with or without fever may in isolated instances give temporary positive serologic reactions. Serologic tests should therefore be repeated for a sufficiently long period to eliminate the possibility of the fluctuating type of reaction.

DISCUSSION

Dr. Paul Kreitz, Bethlehem, Pa.: The Kline and the Eagle test have almost superseded the Kahn and the Wassermann test in the East.

Dr. Harold B. Rothbart, Ann Arbor, Mich.: The blood may yield a false negative reaction under certain circumstances. Infants born of syphilitic parents may have a negative Kahn reaction, and the reaction may not become positive before the fourth or the sixth month of life. Of course, it is well known that in cases of acquired syphilis the serodiagnostic test may not be positive for several weeks. There is also evidence that during the treatment of latent syphilis the Kahn test may become temporarily negative and then positive again.

Regarding the Kline and the Eagle test, comparative tables indicate that they yield more false positive reactions than the Kahn test. I do not think that I can overemphasize the necessity of repeating serodiagnostic tests. Only too frequently a diagnosis of syphilis is made on a single positive Kahn reaction. The child is put through a course of treatment which disturbs the family and brands him for the rest of his life. No harm is done by waiting until the diagnosis is confirmed.

The One Hour, Two Dose Dextrose Tolerance Test. Dr. M. Cooperstock, Marquette, Mich.

The one hour, two dose dextrose tolerance test introduced by Exton and Rose several years ago offers the distinct advantage of saving time and preserves the specificity of the older methods. The test is suitable for use with infants and children. The micro blood sugar method is of sufficient accuracy and in the case of infants and young children adds simplification to a laboratory method in which the technical difficulty of obtaining blood often constitutes a problem.

The total amount of dextrose to be used is determined on the basis of 1.5 Gm. per kilogram of body weight. Samples of blood and urine are collected while the child is fasting, and immediately thereafter one-half the calculated dose of dextrose is given in a 20 per cent solution. Thirty minutes later a second sample of blood is taken and the remaining dose of dextrose given. One hour after the

first administration of dextrose the last samples of blood and urine are obtained. In the original test, designed for adults, a total dose of 100 Gm. of dextrose in a 15 per cent solution is used. With infants, the dose of dextrose, calculated according to the body weight, should be higher. Two grams per kilogram is the unit used in the calculation.

The criteria for the normal response of the blood sugar are exactly the same as in the older method for the half-hour sample; the rise in the blood sugar level does not exceed 75 Gm. The sugar content of the sixty minute sample of blood may be the same, below or above that of the thirty minute sample. All samples of urine have a negative reaction to Benedict's test.

The diabetic curve with this short method is characterized by a more or less sharp rise in the blood sugar level sixty minutes after the second administration of dextrose. Exton and Rose stipulated that this rise should not be less than 10 mg. above the level for the thirty minute samples, with the sugar content of the blood and the urine in relation to the severity of the disease.

The one hour, two dose dextrose tolerance test was applied to a number of children with diabetes of various grades of severity. A 7 year old girl with early diabetes had a blood sugar content of 107 mg. per hundred cubic centimeters during fasting, of 250 mg. at thirty minutes and of 375 mg. at sixty minutes, with glycosuria evident on examination of only the last specimen.

A boy of 9 years with aglycosuria showed a high blood sugar level, 320 mg. The value for the thirty minute sample was 400 mg. and that for the sixty minute sample 415 mg. The urine showed a 1 plus reaction to the test for sugar. Several diabetic children with a high blood sugar level during fasting and glycosuria showed a fall in the level in the sixty minute sample.

This observation of a decrease in the blood sugar content after the second dose of dextrose was accentuated in several nondiabetic children, the level falling below that during fasting in several instances. This illustrates the previously observed paradoxic hypoglycemic effect of carbohydrate.

MENINGITIS WITH UNUSUAL COMPLICATIONS. DR. MARK OSTERLIN, Traverse City, Mich.

N. P., aged 21 months, was admitted to the Central Michigan Children's Clinic on Aug. 8, 1936, with the typical symptoms of meningitis. Cultures of the blood and the spinal fluid were positive for the meningococcus. When the patient was admitted, slight cloudiness of the right cornea and a small amount of discharge over the conjunctiva were noted. During the next four days the conjunctiva became markedly injected; there was a purulent discharge, and the cornea became cloudy. Pus was noted in the anterior chamber of the right eye on August 11. On August 12 a small amount of pus was removed from the chamber. A smear and culture revealed gram-negative diplococci. The pupil was kept dilated with atropine, and warm packs of boric acid were applied three times daily. On August 15 redness and swelling were noted in the cervical region on the left side. Hot wet dressings were applied. On August 22 the swelling was opened and about 20 cc. of pus removed. Cultures revealed meningococci and staphylococci. Treatment consisted of intravenous and intraspinal injections of antimeningococcus serum and supportive measures. The cloudiness of the cornea gradually disappeared, but examination later revealed exudative retinitis. At the time of discharge, October 18, there was questionable light perception.

DISCUSSION

DR. FRANK VAN SCHOICK, Jackson, Mich: I should like to ask Dr. Osterlin whether he thought the infection of the eye was of hematogenous origin or due to extension. The happenings in the course of meningococcic meningitis are, in spite of treatment with serum, discouraging. In cases of intracranial hemorrhage of the new-born in which encephalography has been carried out for diagnostic purposes, beneficial results have sometimes followed, presumably from the breaking up of adhesions. Some such mechanical means may be of help in complicated

cases. Another important point is the evacuation of any focus that can be found as quickly as possible because of the rapidity with which the meningococcus multiplies.

DR. WILMA SACKS, Ann Arbor, Mich.: The rapidity with which the meningococcus works is well shown in a case I once observed. The patient, a 16 month old boy, was entirely well one evening. During the night he became irritable and restless, and a fever developed. He was brought to the hospital at about 11 the following morning. A few petechial spots were observed, but there was no stiffness of the neck or other sign of meningitis. Meningococci were observed in the blood smear. The patient died at about 2 p. m. A postmortem culture of the cardiac blood was positive for the meningococcus. A postmortem spinal tap showed a clear fluid with only two or three cells. This is a case of marked meningococcic septicemia.

DR. F. J. MELLENCAMP, Ann Arbor, Mich.: A relatively uncommon complication of meningococcic meningitis occurred in a 13 year old boy. Massive arthritis of the left knee developed about the fourteenth day of the disease. Traction was applied, and the condition cleared in about ten days.

DR. M. M. FENTON, Ann Arbor, Mich.: Dr. Osterlin's patient was admitted to the contagious disease unit of the University Hospital on Aug. 30, 1936, twenty-three days after the onset of meningitis. She appeared acutely ill; her temperature was 101 F. and later rose to 104 F. There were marked opisthotonos, inability to respond, subsiding uveitis in the right eye and marked spasticity of all the extremities. The spinal fluid showed an increased cell count on repeated examinations but no positive culture for the meningococcus. However, in view of the marked decrease in the sugar content of the spinal fluid (from 10 to 20 mg. per hundred cubic centimeters) and the increased cell count, activity was still suspected. Accordingly, meningococcus antitoxin totaling 60,000 units was given intravenously and intramuscularly. The temperature soon dropped to normal. Because of the increased pressure, which caused vomiting, repeated spinal taps were needed. The child was given high caloric gavage feedings and multiple transfusions. Prior to her discharge, on October 18, she was able to eat alone and responded well to stimuli. Although still spastic in her lower extremities and blind in her right eye, she appeared markedly improved clinically. With regard to the mechanical treatment referred to by Dr. Van Schoick, it has been the custom at the contagious disease unit for some years to introduce a certain amount of air when serum is given intraspinally. The idea is to break up adhesions that may be forming. It is of course necessary to have the patient in the upright position when the air is injected.

DR. MARK OSTERLIN, Traverse City, Mich.: In answer to Dr. Van Schoick's question, I regarded the condition as a hematogenous infection of the eye. The blood culture was positive. The clinical picture was that of meningococcic septicemia.

FAILURE TO PRODUCE EXPERIMENTAL DENTAL CARIES BY FEEDING DEFICIENT DIETS TO RATS. DR. C. A. LILLY, Ann Arbor, Mich.

There is no agreement regarding the relationship of dental caries to diet. The albino rat was selected as the animal of choice, since it has a food requirement more like that of human beings than any other animal.

Different colonies of rats were fed diets of various known deficiencies, after which they were killed and carefully examined post mortem for dental caries. Except in the second generation, in which the life of the animal was frequently short because of the inadequacy of the diets, no rat that lived less than six months was killed and studied.

The following types of diet were fed: diets deficient in protein, calcium, phosphorus and vitamins and many combinations of these elements; diets high in carbohydrate (66 per cent sucrose, dextrose, lactose and maltose), and diets representing over long periods of time vitamin combinations of many kinds. Rats

fed adulterated diets were not noticeably affected. These diets were fed to over 1,600 rats. While malocclusion, hypoplastic teeth, rickets, skeletal deformities and defects were frequently observed, not a single carious tooth was produced, even in the second generation of these rats.

There is no "accepted" report of the production of dental caries in any animal by a deficient or inadequate diet. Reports have been published in which caries is alleged to have resulted from dietary deficiencies; they have been seriously questioned.

Shelling and Anderson (1936), in a study of 278 children, failed to find vitamin D "a protective against dental caries." The disagreement in the literature as to the effect of vitamin D is so pronounced that one in search of the truth all but despairs.

Dental caries is produced at will in rats with the Hoppert and the Webber and Canniff coarse corn meal diet or with a coarse rice diet; both are unquestionably normal diets. The animals were healthy and attained normal size, weight, reproduction and blood and bone composition; in short, they were normal in every respect except that they had dental caries.

Thus there were two colonies of rats: The animals of one, fed inadequate diets, were physically subnormal in every particular but free from dental caries; those of the other, fed normal diets, were normal in every respect except that they had a high degree of dental caries. The cause of caries in normally fed animals has not yet been determined. However, my co-workers and I are certain that the cause is not of a nutritional nature.

Clinically healthy, robust persons of good dietary habits frequently have a large amount of dental caries, while undersized, underweight persons of poor dietary habits may be entirely free from the condition. This fact was frequently observed in the examinations of young men for military service during the war. Many more young men of the first than of the second type were seen.

The lack of agreement regarding the relation of diet to dental caries, the clinical observations cited and the experimental studies reported prompt one to be guarded in telling patients that dental caries is the result of nutritional deficiencies and that good diets will prevent it.

DISCUSSION

Dr. D. Murray Cowie, Ann Arbor, Mich.: I should like to ask if the reports in the literature do not indicate that the action of vitamin D is confined principally to the deciduous teeth.

Dr. C. A. Lilly, Ann Arbor, Mich.: Yes. Few observers report a marked effect from the use of vitamin D in children over 10 or 12 years of age and none in children past puberty.

Dr. John L. Law, Ann Arbor, Mich.: I should like to ask if Dr. Lilly has tried the effect of a diet high in carbohydrate on rats over a long period.

Dr. C. A. Lilly, Ann Arbor, Mich.: I have fed groups of rats diets high in carbohydrate for as long as one year at a time and failed to produce caries. Unfortunately, Dr. Henry, the bacteriologist, contracted undulant fever before the experiment was completed and of course could not finish the bacteriologic studies. Therefore, nothing is known of the bacteriologic aspect of this experiment.

Dr. F. G. Mellencamp, Ann Arbor, Mich.: Stefansson reported observations he made on Eskimos living on a diet high in fat and in protein in whom no dental caries was found. Some years later he reported a similar study, in which dental caries was found in appreciable amounts. He also observed that a group of South Sea islanders who lived on a diet high in carbohydrate did not have dental caries.

Boric Acid Poisoning in an Infant. Dr. Ernest Watson, Detroit.

A case of fatal boric acid poisoning in a 4½ month old infant is reported. The infant presented typical severe manifestations of infantile eczema on admission to the University Hospital.

The only significant features of the case were the application of approximately 120 Gm. of boric acid ointment U.S.P. to the entire surface of the body on the second and third days in the hospital. Persistent clonic convulsions developed approximately thirty hours after the first application. These convulsive seizures came on at intervals for approximately three days; thereafter the patient remained in a comatose condition until death, two and one-half weeks later. He apparently became blind and deaf soon after the onset of the convulsions.

Significant features of the case were the demonstration of boric acid in the urine and the spinal fluid and the presence of generalized, intense erythema. Treatment consisted, for the most part, of supportive measures and efforts made to hasten elimination of the boric acid.

A brief review of the literature on boric acid poisoning was included in the paper.

DISCUSSION

Dr. George M. Frauenberger, Cincinnati: I worked with Dr. Watson in caring for this baby and was very much interested. A survey of the literature showed that about thirty-one cases in which the outcome was fatal have been reported. Dr. Edmunds stated that a death in this hospital years ago resulted from the dusting of boric acid powder on the large wound of an adult. Dr. Cowie told of a baby who died of the ingestion of a boric acid solution thought to be sterile water. This death resulted in the coloring of all standard solutions used in his wards.

Several lessons are to be learned from Dr. Watson's paper. In the first place, boric acid may be a most potent poison under conditions in which it can be absorbed in fairly large amounts in a relatively short period. Also, boric acid solutions should be colored in a characteristic way, particularly in hospitals, so as to prevent accidental poisoning. This may be done by adding 2 drops of a saturated alcoholic solution of gentian violet to 5 gallons (19 liters) of boric acid solution.

Dr. Harold B. Rothbart, Ann Arbor, Mich.: I recall a case in Chicago. The nurse made a mistake and gave boric acid instead of saline solution. Nothing happened to the baby except the development of an erythematous rash.

Dr. Clement A. Smith, Boston: In reading about boric acid poisoning did Dr. Watson find any therapeutic recommendations?

Dr. Ernest Watson, Detroit: Boric acid poisoning causes an acidosis which is not amenable to ordinary methods of treatment because it is of the "fixed type." I know of no antidote for boric acid poisoning. Treatment in the case reported consisted of intravenous injections of dextrose solutions, blood transfusions and other so-called supportive measures. If they are given early, I have no doubt that alkalis such as sodium lactate might be of value.

"Auto" Passive Transfer of Allergic Antibody. Dr. D. Murray Cowie, Ann Arbor, Mich.

Evidence is presented which tends to show that the skin of a sensitized person which fails to react to the intradermal injection of specific allergen may be made to react by passively transferring the person's own blood serum into his own skin. Twenty-four hours later if substances to which the subject is sensitive are injected intradermally into this "auto" passive transfer area a typical allergic reaction develops. A skin that has been shown to react to a specific allergen often responds more markedly if it has first been treated by the passive transfer of a small amount of the patient's serum. For example, on ordinary intradermal testing, feather allergen gave a reaction of 31 mm., and when it was injected into an "auto" transfer area it induced a reaction of 46 mm. Mushroom allergen on intradermal testing in another person induced a reaction of 19 mm., and when injected into a passive transfer area it induced a reaction with a diameter of 38 mm. In other words, the mechanical introduction of additional antibody into an already sensitive skin may increase the size of the reaction.

When parallel observations are made of the reaction of "auto" passive transfer and ordinary passive transfer areas to specific allergen it is found that the latter

are usually larger. However, the reactions in the "auto" passive transfer areas are definite and typical, measuring up to 46 mm. in average diameter.

No passive transfer examination is reliable unless a series of control observations is made on untreated areas of the recipient's skin. The "auto" passive transfer method eliminates this necessity, for it has already been proved that the patient's skin does not react to the intradermal injection of the allergen.

COSEASONAL INTRADERMAL TREATMENT OF HAY FEVER. DR. B. JIMENEZ, Ann Arbor, Mich.

The object of this paper is to call attention to the advantage of the coseasonal intradermal treatment of hay fever. I have found that if I treat my patients with small daily doses of a weak dilution of specific pollen antigen they secure satisfactory relief. This relief has been noticed in all patients thus far treated, whether it is their first treatment or a continuation of a preseasonal treatment.

The quantity of material injected is small (0.03 or 0.05 cc. of a 1:1,000 or even a 1:5,000 solution); otherwise the same good results are not obtained. My co-workers and I have tried this method in over a hundred cases, with the same result. Not one patient failed to show some improvement. The relief from symptoms is noticed the second or third day of treatment, and it lasts as long as the daily specific treatment is continued. This benefit has no relation to the pollen count in the air.

Dr. E. W. Phillips in 1926 reported that by the intradermal injection of pollen extract in increasing strength "prompt and effective relief from symptoms was obtained." Dr. Grafton T. Brown in 1925 recommended coseasonal treatment of fall hay fever for patients who apply late for treatment. He used increasing doses, and the inference is that the method of injection was subcutaneous. Dr. Warren T. Vaughan in his article "Specific Treatment of Hay Fever During the Attack" recommended daily treatment with specific pollen antigen by subcutaneous injection.

My conclusions are as follows:

1. Coseasonal treatment of patients with hay fever has resulted in immediate and satisfactory improvement in a large percentage of the cases in which it has been tried.

2. A constant daily dose (from 0.03 to 0.05 cc.) of a weak dilution of antigen (1:1,000 or 1:5,000), yielding 200 units, given intradermally is recommended.

3. This plan works equally well with patients who have had preseasonal treatment or no treatment and with persons who have never before been treated by injections of specific antigen.

4. Relief from symptoms is usually noticed after the second or third day of treatment but is lost if the daily injections are discontinued.

FURTHER STUDIES ON DELAYED INTRADERMAL REACTIONS. DR. WILMA SACKS, Ann Arbor, Mich.

Last year certain observations on delayed intradermal reactions were reported. Owing to changes in technic in the sensitization clinic and to the impression that fewer delayed reactions were being observed, a second series of cases was reviewed. A decided decrease in the incidence of delayed reactions was found. The cases may be tabulated as follows:

Condition	First Series (125 Cases) Delayed Reactions, Percentage of Total	Second Series (150 Cases) Delayed Reactions, Percentage of Total
Asthma	23.8	10.5
Eczema	15.0	5.2
Allergic rhinitis	24.4	12.3
Migraine	40.8	20.7
Urticaria	29.8	8.9

In the attempt to find an explanation for these figures, extracts were made by the old and the new method, and both series of extracts were ultrafiltered. Tests were made with standardized and unstandardized extracts and with ultrafiltration residues and filtrates. The tests were made on a small number of patients who had formerly given delayed reactions. None of these extracts or fractions caused any delayed reactions on the test subjects. From these studies it appears that delayed reactions in many instances may be due to impurities in the extracts, the nature of which is still unknown. With purified antigens, the percentage of delayed reactions is greatly reduced and their significance becomes increasingly doubtful.

CRYPTORCHIDISM. EVALUATION OF THERAPY WITH GONADOTROPIC SUBSTANCE: A PRELIMINARY REPORT. DR. JOHN L. LAW, Ann Arbor, Mich.

Of the three available methods of managing undescended testes—operative treatment, therapy with gonadotropic substance and waiting for spontaneous descent—the second method has much to recommend it.

Drake's observation that in most cases of cryptorchidism the testes descend spontaneously at puberty is in variance with the observation of other authorities. Many instances of so-called descent are no doubt examples of "migatory" testes.

Moore's and Pace's work and general clinical experience show that atrophy, aspermia, permanent fixation and development of tumors are more common with undescended testes than with normally placed organs.

Surgical management of undescended testes is not entirely satisfactory. In expert hands successful placement varies from 30 to 90 per cent. Frequently the testes do not develop after the operation.

Experimental evidence gathered by Engle and others demonstrates that injection of the anterior gonadotropic substance from the urine of pregnant women into immature rats and monkeys causes descent of the testes. The interstitial cells of the testes, the seminal vesicles and the external genitals become enlarged. There is no valid evidence that the gonadotropic substance produces any harmful effect on the testes or their adnexa. Since Shapiro showed that the gonadotropic substance causes descent of the testes in man, other investigators have used this form of therapy. In eighty-six, or 70 per cent, of 123 cases of unilateral or bilateral cryptorchidism in boys between 1 and 15 years of age treated by twelve investigators during the last five years, descent of the testes occurred; partial descent took place in seven, or 5.7 per cent, and failure in thirty, or 24.3 per cent. In many cases the secondary effects included increase in the size of the testes, scrotum and penis, acceleration of the body growth and improvement in the mental outlook. In no instance were signs of atrophy of the testes or adnexa noted.

During the past two years eight boys were treated in the University Hospital with the gonadotropic substance from the urine of pregnant women. Descent of the testes took place in six, or 75 per cent. The two boys with whom the therapy failed are still under treatment. No local or general reactions occurred, and there were no harmful effects.

From the recorded experience of other observers and the observations of myself and my co-workers, it appears that the injection of gonadotropic substance offers a safe, convenient and effective method of treating cryptorchidism in boys. In cases in which operative correction is advisable for mechanical reasons, the judicious use of gonadotropic substance before and after the operation might effect normal development of the testes and penis.

AMAUROTIC FAMILY IDIOCY IN A FINNISH INFANT. DR. DON A. COWAN and DR. M. COOPERSTOCK, Marquette, Mich.

Amaurotic family idiocy, originally thought to be limited to the Jewish race, is occasionally seen in persons of other races. Several such instances have been confirmed by the characteristic changes in the brain observed at postmortem examination. A case is reported of the infantile type of Tay-Sachs' disease in a 10 month old baby whose parents were of pure Finnish stock.

Patient P. P., aged 10 months, a normal baby born at full term, apparently developed normally to about the eighth month, when she began to be weak. She had learned to sit erect at the age of 6½ months; this ability was lost at 8 months. The weakness progressed during the next two months; she was unable to hold up her head and was no longer attentive to her surroundings. Examination showed an obese, flabby, listless baby, with little reaction to her environment. Vision appeared entirely lost. Ophthalmoscopic examination revealed extremely white disks. At the macular regions a grayish white area, about 1 disk diameter in width, with a cherry-red spot in the center, was present. The spleen was felt 2 fingerbreadths below the costal margin. Routine laboratory examinations gave normal results except that leukocytosis was observed; there were 23,000 white cells, with 54 per cent neutrophils. Histologic examination of material obtained by splenic puncture failed to reveal any of the characteristics of Niemann-Pick's disease.

Amaurotic family idiocy has been separated into two main types, infantile and juvenile. The former usually occurs soon after the sixth month, is steadily progressive and is characterized chiefly by a steady loss of muscle power, mental deterioration and loss of vision, with eventual blindness. Extreme weakness, apathy and often convulsions are features of the terminal picture, which usually ensues within a year. The funduscopic findings are usually the outstanding diagnostic features of the disease. The cherry-red spot at the location of the macula lutea, surrounded by a larger milky blue area, and more or less atrophy of the optic nerve are characteristic. The juvenile form usually occurs after the sixth year and is also progressive and fatal. Children afflicted with it may, however, live for many years.

The pathologic changes in the brain and the spinal cord in this disease are striking and typical. Because the ophthalmoscopic and pathologic changes in the central nervous system are identical with those sometimes found in Niemann-Pick's disease, the condition is thought to belong in the group of lipoid degenerative diseases. Its familial nature is well known.

Book Reviews

School Health Problems. By Dr. Laurence B. Chenoweth and Dr. Theodore K. Selkirk. Price, $3. Pp. 387, with 112 illustrations. New York: F. S. Crofts & Co., 1936.

This book is designed for students of education, teachers in service and others who may desire a knowledge of the fundamentals of school health problems. It should be of interest to pediatricians who may participate in school programs or give guidance to this branch of community service. It is more concerned with the problems of the child of school age than it is with the school plant, the management of the curriculums and the hours and methods of instruction, which should be designed to meet the individual needs of children from the standpoint of their physical, mental, emotional and social health. The emphasis is generally on the knowledge which the well trained physician brings to bear on school problems rather than on the problems of the administration of health measures in school and the methods of education of the child in healthful living. The book covers in a brief form and brings up to date much of the kind of material so thoroughly reviewed by Dr. James Kerr, of the London county council, in 1926 in his large book, "The Fundamentals of School Health." The bibliography at the end of each chapter provides extensive material for further study, and it should be useful in its particular field.

"School Health Administration," by Dr. Richard M. Bolt, is presented only in outline form, but the author's eight principles of sound administration deserve mention.

The discussion of the place of the physical examination in school programs is a distinct contribution. The authors make clear the limitations of such an examination and the desirability of continuous supervision of health by a personal physician. They wisely point out that when an effort is not made to have personal supervision by a physician many parents rely too much on the school examinations. They emphasize education in health as the "major objective" of the school physical examination. Although they refer to some of the possibilities of education in the health of the child and the parent through the physical examination, it is the opinion of the reviewer that school examinations will continue to neglect this "major objective" until some one points the way more definitely and emphatically. Obviously, the school physician cannot effectively teach the many hundreds of children and parents who appear before him in school, so he must have the assistance of a nurse and a teacher if the examination is to be truly educational. With a more thorough recognition of the importance of education in the medical supervision of health, the teachers should be able to influence the attitude of the children, and the physician should be able to point out many practical opportunities for influencing this attitude by illustrating the need for preventive medicine.

While the discussion of the school physical examination contributes so much regarding a sound policy on this generally confused subject, the authors appear to confuse further the questions of the function of the school with respect to the more serious physical defects. Of course, the reviewer agrees with the authors that if one is to use the term correction of defects in a general sense it should be used "to denote action leading toward the satisfactory handling of a defect rather than bringing of the child up to normal." They say: "Intensive follow-up on the more serious defects may secure the correction of a greater percentage of the defects selected for follow-up than is now the case; but it is possible that greater good may result from the correction of a smaller percentage of defects in a large total number. In some ways health work in schools is like advertising; a small percentage of responses to an advertisement reaching a large number of people may bring larger returns than more intensive salesmanship devoted to fewer people. It is not the percentage but the total number of corrections of

significant defects that is important. From his point of view the wholesale examination of children and simple notification of parents may not be so unproductive as a study of the percentage of corrections might indicate." This statement is true, but it fails to recognize the need for greater emphasis on the more serious physical defects which is common in many school systems. The authors apparently misunderstand the problem to which they refer in "Physical Defects— the Pathway to Correction," by the American Child Health Association.

The emphasis on the more severe physical defects is necessary because "the school must . . . protect its supporters, the taxpayers, against wasteful expenditure of educational funds," as pointed out by Dr. W. W. Bauer, when he refers to the waste and impaired efficiency due to severe physical handicaps. It is necessary, also, because such a large proportion of seriously handicapped children require expensive follow-up care by the nurse and so often the nurse must select those to whom she will give such care, for her schedule prevents her giving it to all. Furthermore, the wholesale examination of children in school without the examiner's having an opportunity to know the children thoroughly is more likely to result in errors in the selection of defects in the less severely handicapped children when the emphasis is not placed on the really handicapping defects. Where there are adequate facilities for follow-up care and for adequate discrimination in the selection of the defects, no doubt there should be no such emphasis on the severe defects, and it is appropriate that general advertising of the importance of medical supervision should be part of the school program.

Problems of Encephalography in Childhood. Preface by S. A. Reynberg. Price, 6 rubles. Pp. 105, with 137 tables and illustrations. Leningrad: Bio-Medical Publishing Company, 1936.

The technic of encephalography is discussed by M. A. Toporikova. The lumbar route for the injection of air is considered preferable except for children with edema or trauma of the brain, for whom ventriculography is suggested. A sitting position for the patient is recommended in order that he may avoid the shock to the nervous system which occurs if the position is changed when the roentgenograms are taken. A special suspension bandage is recommended to keep the head in the proper position. Encephalography with the child's head hanging down is of great diagnostic value, for this position increases the visualization of the third ventricle and cistern.

A discussion of the interpretation of encephalograms, by D. C. Lindenbraten, is based on the study of an extensive series of cases correlated in some instances with a postmortem examination. The author thinks that the measurement of the brain by encephalograms is of no great value. The appearance of the brain when the walls of the ventricles are abnormal and in various other pathologic conditions is described. Change in the shape of the ventricles is thought to be of more diagnostic significance than change in size.

Clinical and roentgenologic observations on diseases of the central nervous system in children are discussed by D. C. Lindenbraten and N. N. Keller. The authors describe in detail encephalograms made during several diseases, correlating the clinical symptoms observed. The conditions studied fall into the following groups: (1) epilepsy, pyknolepsy, etc., with the encephalograms showing nothing abnormal, (2) postmeningitic conditions, (3) postencephalitic conditions, (4) postmeningo-encephalitic conditions and (5) developmental defects. Children with and without psychic changes were studied. The psychic and motor changes were worse in children who had had inflammation or a toxic condition of the brain than in those with developmental defects. Only in rare instances was trauma done at birth shown by encephalogram. Among the conditions discussed are tumor, microcephaly, hydrocephaly, hemiplegia and various motor disturbances.

Clinical, roentgenologic and encephalographic observations during epilepsy and pyknolepsy in children are described by D. C. Lindenbraten and N. N. Keller. The encephalograms of epileptic and pyknoleptic children showed that there are

no typical encephalographic changes in epilepsy and that the changes present are due in part to certain preceding pathologic conditions. For children with epileptic disease the percentage of roentgenograms showing nothing abnormal was highest between the ages of 1½ and 2 years. Ninety-six per cent of the older children with epilepsy and an associated neurologic disturbance, such as hemiplegia, showed some organic pathologic condition of the brain substance. The types of epilepsy in children are discussed, and roentgenograms of patients with different disturbances of the central nervous system are presented. The fact is stressed that patients with spastic disease or hemiplegia do not tolerate encephalography well. In some cases a therapeutic effect of encephalography was noted. In general, when organic change was present less therapeutic effect was observed than when it was not.

The book includes a number of diagrams of the central nervous system as well as numerous encephalograms of the normal and the pathologic brain.

The bibliography is not complete, but the book should be widely useful in Russian clinics.

Nature and Treatment of Amentia. By L. Pierce Clark. Price, $2.50. Pp. 306, with 1 illustration. Baltimore: William Wood & Company, 1933.

This book is a summary of a long series of studies of amentia from a psychoanalytic point of view. The author states that "our interest centers mainly upon understanding the individual as a human being; upon studying his attempts to get along in the world, and upon learning in what ways we may help him to function more successfully."

An introductory chapter is devoted to an excellent summary of psychoanalytic principles. The remainder of the book is devoted largely to studies of cases, the attempt being made to correlate and explain the behavior of persons with varying degrees of amentia in terms of psychoanalytic principles. Cases are described illustrating the various destructive instincts, primary and secondary narcissism, reactions to parents, castration anxiety and other psychic factors. The conclusion and analyses are made from purely objective observations. The author describes in detail the behavior which led to the interpretations. The reader can, therefore, decide for himself whether the conclusions are warranted. The book is extremely well written, interesting and clear. It should be read by every one interested in the management of feebleminded children.

Diseases in Childhood, A Clinical Study. By Robert S. Frew, M.D. Price, $11. Pp. 669, with 89 illustrations. New York: The Macmillan Company, 1936.

Whatever may be said of this book, it is certainly different. It takes up the first year of life, and this is divided into three sections, from birth to 1 month, from 1 month to 6 months and from 6 months to 1 year. Each of the diseases is treated briefly in each section. The author has recorded his experience in seeing outpatients at the Great Ormond Street Hospital, London, for a period of twenty-five years. He states that he has analyzed 8,823 consecutive cases. Some of the book appears rather too short to be adequate. The author has coined a new word, "hyperphlebaemia," which he defines as "an excessive quantity of blood forced into the intracorporeal venous system during birth before it is ready to receive it." He evidently attaches great importance to this condition, since he discusses in connection with it no fewer than forty-six definite clinical entities. The book is well printed, and the illustrations, while not numerous, are good. Occasional case histories are reported. This is not a textbook in the ordinary sense of the term but rather a record of clinical experience.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Herreplein, Groningen, Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini, 24, Rome, Italy.
Secretary: Professor Vitetti, Rome Italy.
Place: Rome, Italy. Time: Sept. 27-30, 1937.

American Committee:
Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. L. Emmett Holt Jr., Johns Hopkins Hosp., Baltimore.

Canadian Committee:
Chairman: Dr. H. B. Cushing, 1390 Sherbrooke St., W., Montreal.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St., W., Montreal.

International Congress for the Protection of Children

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.
Place: Rome, Italy. Time: Oct. 4-8, 1937.

FOREIGN

British Paediatric Association

President: Dr. Leonard Findlay, 14 Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Lancelot Barrington-Ward, 85 Harley St., London, W. 1.
Secretary: Dr. K. H. Tallerman, 122 Harley St., London, W. 1.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv, Palestine.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv, Palestine.

Sociedad Cubana de Pediatría

President: Prof. Félix Hurtado Galtés, Carlos III, 7, Havana.
Secretary: Dr. Carlos Hernández Miyares, San Lazaro 370, Havana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Havana. Time: Third Thursday of every month.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: Atlantic City, N. J. Time: June 7-11, 1937.

American Academy of Pediatrics

President: Dr. Laurence R. DeBuys, 1417 Delachaise St., New Orleans, La.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: Waldorf-Astoria Hotel, New York. Time: June 3, 4 and 5, 1937.
Region I. Place: Boston, Mass. Time: Nov. 12-13, 1937.
Region II. Place: New Orleans, La. Time: Nov. 30, Dec. 1-3, 1937.
Region III. Place: Lake Shore Athletic Club, Chicago. Time: Nov. 4-6, 1937.
Region IV. Place: Los Angeles, Calif. Time: October 1937.

American Hospital Association, Children's Hospital Section

Chairman: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Secretary: Miss Edith F. Bateman, Shriners' Hospital for Crippled Children, St. Louis, Mo.

American Pediatric Society

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: The Homestead, Hot Springs, Va. Time: April 29-30 and May 1, 1937.

Canadian Society for the Study of Diseases of Children

President: Dr. A. P. Hart, 1844 Bloor St., W., Toronto, Ont.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

Society for Pediatric Research

President: Dr. Francis Scott Smyth, University of California Medical School, San Francisco.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.
Place: Chalfonte-Haddon Hall, Atlantic City, N. J. Time: May 4, 1937.

SECTIONAL

North Pacific Pediatric Society

President: Dr. D. M. Dayton, Medical Arts Bldg., Tacoma, Wash.
Secretary: Dr. H. T. Clay, Medical Arts Bldg., Tacoma, Wash.
Place: Portland, Ore. Time: June 1937.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Gilbert Levy, 20 S. Dunlap St., Memphis, Tenn.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.

STATE

Alabama Pediatric Society

President: Dr. Wallace A. Clyde, Employees' Hospital, Fairfield.
Secretary-Treasurer: Dr. M. G. Neely, Employees' Hospital, Fairfield.
Place: Birmingham. Time: April 19, 1937.

Arkansas State Pediatric Association

Chairman: Dr. A. C. Kirby, 701 Main St., Little Rock.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.

Florida State Pediatric Society

President: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Miami.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. Mercer Blanchard, 1301 Broadway, Columbus.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Howard W. Brayton, 179 Allyn St., Hartford.
Secretary: Dr. Joseph L. Hetzel, 103 N. Main St., Waterbury.

Indiana State Pediatric Society

President: Dr. Ernest R. Carlo, 2902 Fairfield Ave., Fort Wayne.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

Louisiana State Pediatric Society

President: Dr. Edwin A. Socola, 2000 Tulane Ave., New Orleans.
Secretary-Treasurer: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.

Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison, 319 E. Capitol Pl., Jackson.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. Leroy J. Butler, 405 N. Spring St., Winston-Salem.
Secretary: Dr. C. A. Street, 405 N. Spring St., Winston-Salem.

Oklahoma State Pediatric Society

President: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.
Secretary: Dr. Hugh C. Graham, 1501 S. Baltimore Ave., Tulsa.
Place: Tulsa: Time: May 10-11, 1937.

Pennsylvania Medical Society, Pediatric Section

Chairman: Dr. Joseph Stokes, Children's Hospital, Philadelphia.
Secretary: Dr. Theodore O. Elterich, 310 Medical Arts Bldg., Pittsburgh.

South Carolina Pediatric Society

President: Dr. Leland B. Salters, 317 S. Warley St., Florence.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

Tennessee State Pediatric Society

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.

Texas Pediatric Society

President: Dr. George B. Cornick, 507½ E. Houston St., San Antonio.
Secretary-Treasurer: Dr. F. H. Lancaster, 1507 Medical Arts Bldg., Houston.

Virginia Pediatric Society

President: Dr. Basil B. Jones, 1028 W. Franklin St., Richmond.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. John T. Thornton, 58, 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. D. Pilcher, City Hospital, Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

Bronx Pediatric Society

President: Dr. Daniel J. Dolan, 420 E. 159th St., New York.
Secretary: Dr. Samuel T. Levethan, 254 E. 184th St., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Thurman B. Givan, 115 Remsen St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vasder Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. Robert Black, Del Prado Hotel, Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. John Young, 3930 McKinney Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3622 Fairmount Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. Edward A. Wishropp, 10 Peterboro St., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Walter F. Qualtrough, 920 Westheimer Ave., Houston, Texas.
Secretary-Treasurer: Dr. Allan Bloxsom, 4402 Travis St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385 Twenty-Fourth St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. W. R. Moore, 620 Francis St., St. Joseph.
Secretary: Dr. F. S. Hogue, 1103 Grand Ave., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Edwin F. Patton, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Harry Apfel, 988 Park Pl., Brooklyn.
Secretary: Dr. Max Palinsky, 1270, 45th St., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC., SECTION ON PEDIATRICS

Chairman: Dr. W. C. A. Steffen, 42 Union St., Flushing, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144, 38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. Clyde V. Croswell, 1052 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. David W. Goltman, 1073 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. George F. Kelly, 425 E. Wisconsin St., Milwaukee.
Secretary: Dr. Helen Jane Zillmer, 781 N. Jefferson St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Henry E. Utter, 122 Waterman St., Providence, R. I.
Secretary-Treasurer: Dr. Henry E. Gallup, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Secretary: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. A. V. Stoesser, University Hospital, Minneapolis.
Secretary: Dr. Roger L. J. Kennedy, Mayo Clinic, Rochester, Minn.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

OKLAHOMA CITY PEDIATRIC SOCIETY

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Alternate months.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Emily Bacon, 2104 Spruce St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. Lee E. Sutton, Jr., 2601 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. Louise Fry Galvin, 2416 Stuart Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Secretary: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

Rocky Mountain Pediatric Society

President: Dr. James E. Russell Jr., 820 Metropolitan Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. John Zahorsky, 536 N. Taylor Ave., St. Louis.
Secretary-Treasurer: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Frank H. Douglass, Medical Dental Bldg., Seattle.
Secretary: Dr. C. Lu Verne Smith, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. M. Cooperstock, Northern Michigan Children's Clinic, Marquette.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. Louis V. Waldron, 149 N. Broadway, Yonkers, N. Y.
Secretary-Treasurer: Dr. Fairfax Hall, 421 Huguenot St., New Rochelle, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, October, December, February and April.